

=> e andersen peter/au

E1 9 ANDERSEN PERNILLE/AU  
E2 1 ANDERSEN PETE/AU  
E3 371 --> ANDERSEN PETER/AU  
E4 6 ANDERSEN PETER A/AU  
E5 1 ANDERSEN PETER ANDREAS/AU  
E6 5 ANDERSEN PETER B/AU  
E7 62 ANDERSEN PETER C/AU  
E8 1 ANDERSEN PETER CHRISTIAN/AU  
E9 3 ANDERSEN PETER CRAIG/AU  
E10 65 ANDERSEN PETER E/AU  
E11 2 ANDERSEN PETER ESKIL/AU  
E12 1 ANDERSEN PETER ESKILD/AU

=> s e3-e12 and tuberculosis

L1 275 ("ANDERSEN PETER"/AU OR "ANDERSEN PETER A"/AU OR "ANDERSEN PETER ANDREAS"/AU OR "ANDERSEN PETER B"/AU OR "ANDERSEN PETER C"/AU OR "ANDERSEN PETER CHRISTIAN"/AU OR "ANDERSEN PETER CRAIG"/AU OR "ANDERSEN PETER E"/AU OR "ANDERSEN PETER ESKIL"/AU OR "ANDERSEN PETER ESKILD"/AU) AND TUBERCULOSIS

=> s l1 and (RD1-orf3)

L2 9 L1 AND (RD1-ORF3)

=> dup rem 12  
PROCESSING COMPLETED FOR L2  
L3 6 DUP REM L2 (3 DUPLICATES REMOVED)

=> d bib ab 1-  
YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1  
AN 2004:490265 CAPLUS  
DN 141:52841  
TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to *M. tuberculosis*, and use thereof as vaccines and in diagnosis  
IN Andersen, Peter; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter Den.  
PA U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.  
SO CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004115211	A1	20040617	US 2003-620246	20030715
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	EP 1998-913536	A3	19980401		
AB	The present invention is based on the identification and characterization of a number of <i>M. tuberculosis</i> derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused				

proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

L3 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2  
AN 2003:696302 CAPLUS  
DN 139:229237  
TI Protein and DNA sequences of antigens from *Mycobacterium* and uses in tuberculosis diagnosis and treatment  
IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Vegerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk  
PA Statens Serum Institut, Den.  
SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003165525	A1	20030904	US 2002-138473	20020502
US 6982085	B2	20060103		
US 6641814	B1	20031104	US 1998-50739	19980330
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI DK 1997-376	A	19970402		
US 1997-44624P	P	19970418		
DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
US 1998-50739	A2	19980330		
DK 1998-1281	A	19981008		
US 2001-791171	B2	20010220		
US 2002-60428	A2	20020129		
EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from *Mycobacterium tuberculosis*. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing *tuberculosis* caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being. The invention related to treating *tuberculosis* using antigens isolated from *Mycobacterium tuberculosis*.

L3 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3  
AN 2003:609858 CAPLUS  
DN 139:163576  
TI *Mycobacterium tuberculosis* antigens for diagnosis, prevention and treatment of infections caused by species of the *tuberculosis* complex  
IN Andersen, Peter; Skjot, Rikke Louise Vinther  
PA Den.  
SO U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of U.S. Ser. No. 289,388, abandoned.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003147897	A1	20030807	US 2001-804980	20010313
US 6991797	B2	20060131		
WO 9501441	A1	19950112	WO 1994-DK273	19940701
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB,				

GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL,  
 NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA  
 RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,  
 BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG  
 EP 1508339 A1 20050223 EP 2004-77505 19940701  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI  
 US 5955077 A 19990921 US 1995-465640 19950605  
 US 6641814 B1 20031104 US 1998-50739 19980330  
 EP 1449922 A2 20040825 EP 2004-76605 19980401  
 EP 1449922 A3 20041117  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI, CY  
 US 2002094336 A1 20020718 US 2001-791171 20010220  
 US 2004013685 A1 20040122 US 2001-872505 20010601  
 PRAI DK 1993-798 A 19930702  
 US 1993-123182 B2 19930920  
 WO 1994-DK273 A2 19940701  
 US 1995-465640 A1 19950605  
 DK 1997-376 A 19970402  
 US 1997-44624P P 19970418  
 DK 1997-1277 A 19971110  
 US 1998-70488P P 19980105  
 US 1998-50739 A3 19980330  
 US 1998-246191 A2 19981230  
 US 1999-289388 B2 19990412  
 US 2001-791171 A2 20010220  
 EP 1994-919574 A3 19940701  
 EP 1998-913536 A3 19980401  
 DK 1999-1020 A 19990713  
 US 1999-144011P P 19990715  
 US 2000-615947 A2 20000713  
 WO 2000-DK398 A2 20000713  
 US 2001-804980 A2 20010313

AB The present invention is based on the identification and characterization of a number of novel *M. tuberculosis* derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and  $\alpha$ -crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

L3 ANSWER 4 OF 6 USPATFULL on STN  
 AN 2003:291011 USPATFULL  
 TI Nucleic acids fragments and polypeptide fragments derived from *M. tuberculosis*  
 IN Andersen, Peter, Br.o slashed.nsh.o slashed.j, DENMARK  
 Nielsen, Rikke, Frederiksberg, DENMARK  
 Oettinger, Thomas, Hellerup, DENMARK  
 Rasmussen, Peter Birk, K.o slashed.benhaven, DENMARK  
 Rosenkrands, Ida, K.o slashed.benhaven, DENMARK  
 Weldingh, Karin, K.o slashed.benhaven, DENMARK  
 Florio, Walter, Frederiksberg, DENMARK  
 PA Statens Serum Institut, Copenhagen, DENMARK (non-U.S. corporation)  
 PI US 6641814 B1 20031104  
 AI US 1998-50739 19980330 (9)  
 PRAI DK 1997-376 19970402  
 US 1997-44624P 19970418 (60)  
 DT Utility  
 FS GRANTED  
 EXNAM Primary Examiner: Swartz, Rodney P  
 LREP Frommer Lawrence & Haug, Kowalski, Thomas J.  
 CLMN Number of Claims: 43  
 ECL Exemplary Claim: 1  
 DRWN 6 Drawing Figure(s); 6 Drawing Page(s)  
 LN.CNT 5870  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB The present invention is based on the identification and

characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L3 ANSWER 5 OF 6 USPATFULL on STN  
AN 2002:178550 USPATFULL  
TI Nucleic acid fragments and polypeptide fragments derived from *M. tuberculosis*  
IN Andersen, Peter, Bronshoj, DENMARK  
Nielsen, Rikke, Frederiksberg C, DENMARK  
Oettinger, Thomas, Hellerup, DENMARK  
Rasmussen, Peter Birk, Kobenhaven O, DENMARK  
Rosenkrands, Ida, Kobenhaven O, DENMARK  
Weldingh, Karin, Kobenhaven N, DENMARK  
Florio, Walter, Frederiksberg C, DENMARK  
PA STATENS SERUM INSTITUT (non-U.S. corporation)  
PI US 2002094336 A1 20020718  
AI US 2001-791171 A1 20010220 (9)  
RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING  
PRAI DK 1997-376 19970402  
DK 1997-1277 19971110  
US 1997-44624P 19970418 (60)  
US 1998-70488P 19980105 (60)  
DT Utility  
FS APPLICATION  
LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151  
CLMN Number of Claims: 53  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Page(s)  
LN.CNT 6134

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L3 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1998:684968 CAPLUS  
DN 129:300060  
TI Novel antigens of *Mycobacterium tuberculosis* culture filtrates and the genes encoding and their diagnostic and prophylactic use  
IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter  
PA Statens Serum Institut, Den.  
SO PCT Int. Appl., 264 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,			

NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,  
 UA, UG, US, UZ, VN, YU, ZW  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
 CM, GA, GN, ML, MR, NE, SN, TD, TG  
 CA 2285625 AA 19981008 CA 1998-2285625 19980401  
 AU 9868204 A1 19981022 AU 1998-68204 19980401  
 AU 740545 B2 20011108  
 EP 972045 A1 20000119 EP 1998-913536 19980401  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 JP 2001515359 T2 20010918 JP 1998-541074 19980401  
 EP 1449922 A2 20040825 EP 2004-76605 19980401  
 EP 1449922 A3 20041117  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI, CY  
 CA 2319380 AA 19990520 CA 1998-2319380 19981008  
 WO 9924577 A1 19990520 WO 1998-DK438 19981008  
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,  
 DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,  
 KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,  
 MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,  
 TT, UA, UG, US, UZ, VN, YU, ZW  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 1029053 A1 20000823 EP 1998-947412 19981008  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 NZ 504951 A 20010629 NZ 1998-504951 19981008  
 AU 750173 B2 20020711 AU 1998-94338 19981008  
 EP 1484405 A1 20041208 EP 2004-77071 19981008  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI, CY  
 PRAI DK 1997-376 A 19970402  
 US 1997-44624P P 19970418  
 DK 1997-1277 A 19971110  
 US 1998-70488P P 19980105  
 EP 1998-913536 A3 19980401  
 WO 1998-DK132 W 19980401  
 EP 1998-947412 A3 19981008  
 WO 1998-DK438 W 19981008  
 AB Culture filtrate antigens of *Mycobacterium tuberculosis* are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.  
 RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> e skjot rikke/au
E1      2     SKJOT R L/AU
E2      9     SKJOT R L V/AU
E3      1 --> SKJOT RIKKE/AU
E4      2     SKJOT RIKKE L V/AU
E5      17    SKJOT RIKKE LOUISE VINTHON/AU
E6      1     SKJOT V/AU
E7      11    SKJOTH C A/AU
E8      5     SKJOTH C AMBELAS/AU
E9      5     SKJOTH CARSTEN AMBELAS/AU
E10     22    SKJOTH F/AU
E11     4     SKJOTH FLEMMING/AU
E12     3     SKJOTH I H E/AU
  
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=> s e1-e5 and mycobact?  
L4 31 ("SKJOT R L"/AU OR "SKJOT R L V"/AU OR "SKJOT RIKKE"/AU OR "SKJO  
T RIKKE L V"/AU OR "SKJOT RIKKE LOUISE VINTHON"/AU) AND MYCOBACT

=> dup rem 14  
PROCESSING COMPLETED FOR L4  
L5 11 DUP REM L4 (20 DUPLICATES REMOVED)

=> d bib ab 1-  
YOU HAVE REQUESTED DATA FROM 11 ANSWERS - CONTINUE? Y/ (N) :y

L5 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1  
AN 2004:59568 CAPLUS  
DN 140:127185  
TI Antigens from **Mycobacterium** as vaccine and uses in tuberculosis  
diagnosis and treatment  
IN Andersen, Peter; Skjot, Rikke Louise Vinther; Okkels, Li Mei  
Meng; Brock, Inger; Oettinger, Thomas  
PA Den.  
SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004013685	A1	20040122	US 2001-872505	20010601
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
WO 2001004151	A2	20010118	WO 2000-DK398	20000713
WO 2001004151	A3	20010712		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2003147897	A1	20030807	US 2001-804980	20010313
US 6991797	B2	20060131		
PRAI DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
US 1998-246191	B2	19981230		
DK 1999-1020	A	19990713		
US 1999-144011P	P	19990715		
US 2000-615947	A2	20000713		
WO 2000-DK398	A2	20000713		
US 2001-804980	A2	20010313		
DK 1993-798	A	19930702		
US 1993-123182	B2	19930920		
WO 1994-DK273	A2	19940701		
US 1995-465640	A1	19950605		
DK 1997-376	A	19970402		
US 1997-44624P	P	19970418		
US 1998-50739	A3	19980330		
EP 1998-913536	A3	19980401		
US 1999-289388	B2	19990412		
US 2001-791171	A2	20010220		
AB	The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and RD1-ORF5, from <b>Mycobacterium</b> tuberculosis. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the			

polypeptides. The invention related to diagnosing tuberculosis caused by virulent **mycobacteria** in an animal, including a human being.  
The invention related to treating tuberculosis using antigens isolated from **Mycobacterium tuberculosis**.

L5 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2  
AN 2003:696302 CAPLUS  
DN 139:229237  
TI Protein and DNA sequences of antigens from **Mycobacterium** and uses in tuberculosis diagnosis and treatment  
IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Vegerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk  
PA Statens Serum Institut, Den.  
SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003165525	A1	20030904	US 2002-138473	20020502
US 6982085	B2	20060103		
US 6641814	B1	20031104	US 1998-50739	19980330
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI DK 1997-376	A	19970402		
US 1997-44624P	P	19970418		
DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
US 1998-50739	A2	19980330		
DK 1998-1281	A	19981008		
US 2001-791171	B2	20010220		
US 2002-60428	A2	20020129		
EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from **Mycobacterium tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing tuberculosis caused by virulent **mycobacteria**, e.g. by **Mycobacterium tuberculosis**, **Mycobacterium africanum** or **Mycobacterium bovis**, in an animal, including a human being. The invention related to treating tuberculosis using antigens isolated from **Mycobacterium tuberculosis**.

L5 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3  
AN 2003:609858 CAPLUS  
DN 139:163576  
TI **Mycobacterium tuberculosis** antigens for diagnosis, prevention and treatment of infections caused by species of the tuberculosis complex  
IN Andersen, Peter; Skjot, Rikke Louise Vinther  
PA Den.  
SO U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of U.S. Ser. No. 289,388, abandoned.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003147897	A1	20030807	US 2001-804980	20010313
US 6991797	B2	20060131		
WO 9501441	A1	19950112	WO 1994-DK273	19940701

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB,  
 GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL,  
 NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA  
 RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,  
 BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

EP 1508339 A1 20050223 EP 2004-77505 19940701  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI

US 5955077	A	19990921	US 1995-465640	19950605
US 6641814	B1	20031104	US 1998-50739	19980330
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI, CY

US 2002094336	A1	20020718	US 2001-791171	20010220
US 2004013685	A1	20040122	US 2001-872505	20010601

PRAI DK 1993-798 A 19930702  
 US 1993-123182 B2 19930920  
 WO 1994-DK273 A2 19940701  
 US 1995-465640 A1 19950605  
 DK 1997-376 A 19970402  
 US 1997-44624P P 19970418  
 DK 1997-1277 A 19971110  
 US 1998-70488P P 19980105  
 US 1998-50739 A3 19980330  
 US 1998-246191 A2 19981230  
 US 1999-289388 B2 19990412  
 US 2001-791171 A2 20010220  
 EP 1994-919574 A3 19940701  
 EP 1998-913536 A3 19980401  
 DK 1999-1020 A 19990713  
 US 1999-144011P P 19990715  
 US 2000-615947 A2 20000713  
 WO 2000-DK398 A2 20000713  
 US 2001-804980 A2 20010313

AB The present invention is based on the identification and characterization of a number of novel M. tuberculosis derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and  $\alpha$ -crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

LS ANSWER 4 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4  
 AN 2002:906996 CAPLUS

DN 138:13499

TI Hybrids of M. tuberculosis antigens used as vaccines  
 IN Andersen, Peter; Olsen, Anja Weinreich; Skjot, Rikke Louise  
 Vinther; Rasmussen, Peter Birk

PA Den.

SO U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 246,191, abandoned.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
PI US 2002176867	A1	20021128	US 2001-805427	20010313
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI, CY

PRAI US 1997-44624P P 19970418  
 DK 1997-1277 A 19971110  
 US 1998-70488P P 19980105  
 US 1998-246191 B2 19981230  
 DK 1997-376 A . 19970402

AB EP 1998-913536 A3 19980401  
The invention discloses fusion proteins consisting of T cell epitopes derived from the immunodominant antigens ESAT-6 and Ag85B from **Mycobacterium tuberculosis** or homologs thereof, and a tuberculosis vaccine based on the fusion proteins, which induces efficient immunol. memory. It is preferred that the sequences of the first and second T cell epitopes each have a sequence identity of at least 70% with the natively occurring sequence in the proteins from which they are derived. In the most preferred embodiment, the fusion polypeptide comprises ESAT-6 fused to Ag85B wherein ESAT-6 is fused to the C terminus of Ag85B. In one embodiment, there are nitric oxide linkers introduced between the 2 amino acid sequences constituting the parent polypeptide fragments.

L5 ANSWER 5 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 5  
AN 2002:559608 BIOSIS  
DN PREV200200559608  
TI Epitope mapping of the immunodominant antigen TB10.4 and the two homologous proteins TB10.3 and TB12.9, which constitute a subfamily of the esat-6 gene family.  
AU Skjot, Rikke Louise Vinther; Brock, Inger; Arend, Sandra M.; Munk, Martin E.; Theisen, Michael; Ottenhoff, Tom H. M.; Andersen, Peter [Reprint author]  
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark  
pa@ssi.dk  
SO Infection and Immunity, (October, 2002) Vol. 70, No. 10, pp. 5446-5453.  
print.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 30 Oct 2002  
Last Updated on STN: 30 Oct 2002  
AB The human T-cell recognition of the low-molecular-mass culture filtrate antigen TB10.4 was evaluated in detail. The molecule was strongly recognized by T cells isolated from tuberculosis (TB) patients and from BCG-vaccinated donors. The epitopes on TB10.4 were mapped with overlapping peptides and found to be distributed throughout the molecule. The broadest response was found in TB patients, whereas the response in BCG-vaccinated donors was focused mainly toward a dominant epitope located in the N terminus (amino acids 1 to 18). The gene encoding TB10.4 was found to belong to a subfamily within the esat-6 family that consists of the three highly homologous proteins TB10.4, TB10.3, and TB12.9 (Rv0288, Rv3019c, and Rv3017c, respectively). Southern blot analysis combined with database searches revealed that the three members of the TB10.4 family were present only in strains of the **Mycobacterium tuberculosis** complex, including BCG, and *M. kansasii*, whereas other atypical mycobacteria had either one (*M. avium*, *M. intracellulare*, and *M. marinum*) or none (*M. scrofulaceum*, *M. fortuitum*, and *M. szulgai*) of the genes. The fine specificity of the T-cell response to the three closely related esat-6 family members was markedly different, with only a few epitopes shared between the molecules. Minimal differences in the amino acid sequence translated into large differences in recognition by T cells and secretion of gamma interferon. In general, the peptides from TB10.4 stimulated the largest responses, but epitopes unique to both TB10.3 and TB12.9 were found. The relevance of the findings for TB vaccine development and as a potential mechanism for immune evasion is discussed.

L5 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2001:50676 CAPLUS  
DN 134:114829  
TI Tuberculosis vaccine and diagnostics based on the **Mycobacterium** tuberculosis esat-6 gene family  
IN Andersen, Peter; Skjot, Rikke  
PA Statens Serum Institut, Den.  
SO PCT Int. Appl., 80 pp.  
CODEN: PIXXD2  
DT Patent  
LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2378763	AA	20010118	CA 2000-2378763	20000713
	AU 2000059664	A5	20010130	AU 2000-59664	20000713
	AU 779495	B2	20050127		
	EP 1200466	A2	20020502	EP 2000-945660	20000713
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003510018	T2	20030318	JP 2001-509760	20000713
	US 2004013685	A1	20040122	US 2001-872505	20010601
	AU 2005201767	A1	20050519	AU 2005-201767	20050427
PRAI	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	AU 2000-59664	A3	20000713		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	W	20000713		
	US 2001-804980	A2	20010313		

AB The authors report the cloning and T-cell-stimulatory activity of members of the esat-6 gene family of *Mycobacterium tuberculosis*.

L5 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 6

AN 2001:534626 BIOSIS

DN PREV200100534626

TI Antigen discovery and tuberculosis vaccine development in the post-genomic era.

AU Skjot, Rikke Louise Vinther; Agger, Else Marie; Andersen, Peter [Reprint author]

CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark

SO Scandinavian Journal of Infectious Diseases, (2001) Vol. 33, No. 9, pp. 643-647. print.

CODEN: SJIDB7. ISSN: 0036-5548.

DT Article

LA English

ED Entered STN: 14 Nov 2001

Last Updated on STN: 23 Feb 2002

AB For a number of years, a major effort has been put into the identification of candidate molecules for inclusion in a novel vaccine against tuberculosis. Various techniques have been exploited and have resulted in the identification of immunologically important antigens such as the immunodominant antigens ESAT-6 and antigen 85A/B. Today, the availability of the total nucleotide sequence of the *Mycobacterium tuberculosis* genome enables a post-genomic antigen discovery approach based on denotation and screening of complete protein families containing immunodominant molecules. One group of genes sharing properties with ESAT-6 constitute what has been called the esat-6 gene family. The genes have 10-35% homology to esat-6, are approximately the same size and share genomic organization. The data accumulated so far demonstrate that these molecules are immunodominant antigens strongly recognized in human TB patients and with the potential for a novel TB vaccine.

L5 ANSWER 8 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2003:208455 BIOSIS

DN PREV200300208455  
 TI Antigen discovery and tuberculosis vaccine development in the post-genomic era.  
 AU Skjot, Rikke Louise Vinther; Agger, Else Marie; Andersen, Peter [Reprint Author]  
 CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark  
 SO Scandinavian Journal of Infectious Diseases, (2001) No. Special Issue, pp. 79-83. print.  
 CODEN: SJIDB7. ISSN: 0036-5548.  
 DT Article  
 General Review; (Literature Review)  
 LA English  
 ED Entered STN: 30 Apr 2003  
 Last Updated on STN: 30 Apr 2003  
 AB For a number of years, a major effort has been put into the identification of candidate molecules for inclusion in a novel vaccine against tuberculosis. Various techniques have been exploited and have resulted in the identification of immunologically important antigens such as the immunodominant antigens ESAT-6 and antigen 85A/B. Today, the availability of the total nucleotide sequence of the *Mycobacterium* tuberculosis genome enables a post-genomic antigen discovery approach based on denotation and screening of complete protein families containing immunodominant molecules. One group of genes sharing properties with ESAT-6 constitute what has been called the esat-6 gene family. The genes have 10-35% homology to esat-6, are approximately the same size and share genomic organization. The data accumulated so far demonstrate that these molecules are immunodominant antigens strongly recognized in human TB patients and with the potential for a novel TB vaccine.

L5 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2000:260319 CAPLUS  
 DN 132:292711  
 TI Tb vaccine and diagnostic based on antigens from the *Mycobacterium* tuberculosis cell  
 IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Vegerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rosenkrands, Ida  
 PA Statens Serum Institut, Den.  
 SO PCT Int. Appl., 126 pp.  
 CODEN: PIXXD2

DT Patent  
 LA English  
 FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000021983	A2	20000420	WO 1999-DK538	19991008
	WO 2000021983	A3	20001123		
		W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW		
		RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	CA 2346218	AA	20000420	CA 1999-2346218	19991008
	AU 9960784	A1	20000501	AU 1999-60784	19991008
	AU 766093	B2	20031009		
	EP 1117683	A2	20010725	EP 1999-947257	19991008
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, IE, SI, LT, LV, FI, RO			

PRAI DK 1998-1281 A 19981008  
 US 1999-116673P P 19990121  
 WO 1999-DK538 W 19991008

AB The present invention relates to substantially pure polypeptides, which has a sequence identity of at least 80 % to an amino acid sequence disclosed, or which is a subsequence of at least 6 amino acids thereof, preferably a B- or T-cell epitope of the polypeptides disclosed. The

polypeptide or the subsequence thereof has at least one of nine properties. The use of the disclosed polypeptides in medicine is disclosed, preferably as vaccine or diagnostic agents relating to virulent *Mycobacterium*. The invention further relates to the nucleotide sequences disclosed and the nucleotide sequences encoding the disclosed polypeptides. Medical and non-medical use of the nucleotide sequences is disclosed.

L5 ANSWER 10 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 7

AN 2000:349404 BIOSIS

DN PREV200000349404

TI Detection of active tuberculosis infection by T cell responses to early-secreted antigenic target 6-kDa protein and culture filtrate protein 10.

AU Arend, Sandra M. [Reprint author]; Andersen, Peter; van Meijgaarden, Krista E.; Skjot, Rikke L. V.; Subronto, Yanri W.; van Dissel, Jaap T.; Ottenhoff, Tom H. M.

CS Dept. of Infectious Diseases, C5P, Leiden University Medical Center, 2300 RC, Leiden, Netherlands

SO Journal of Infectious Diseases, (May, 2000) Vol. 181, No. 5, pp. 1850-1854. print.  
CODEN: JIDIAQ. ISSN: 0022-1899.

DT Article

LA English

ED Entered STN: 16 Aug 2000  
Last Updated on STN: 7 Jan 2002

AB The purified protein derivative (PPD) skin test has no predictive value for tuberculosis (TB) in *Mycobacterium bovis* bacillus Calmette-Guerin (BCG)-vaccinated individuals because of cross-reactive responses to nonspecific constituents of PPD. T cell responses to early-secreted antigenic target 6-kDa protein (ESAT-6) and the newly identified culture filtrate protein 10 (CFP-10), 2 proteins specifically expressed by *M. tuberculosis* (MTB) but not by BCG strains, were evaluated. Most TB patients responded to ESAT-6 (92%) or CFP-10 (89%). A minority of BCG-vaccinated individuals responded to both ESAT-6 and CFP-10, their history being consistent with latent infection with MTB in the presence of protective immunity. No responses were found in PPD-negative controls. The sensitivity and specificity of the assay were 84% and 100%, respectively, at a cutoff of 300 pg of interferon-gamma/mL. These data indicate that ESAT-6 and CFP-10 are promising antigens for highly specific immunodiagnosis of TB, even in BCG-vaccinated individuals.

L5 ANSWER 11 OF 11 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 8

AN 2000:104643 BIOSIS

DN PREV20000104643

TI Comparative evaluation of low-molecular-mass proteins from *Mycobacterium tuberculosis* identifies members of the ESAT-6 family as immunodominant T-cell antigens.

AU Skjot, Rikke Louise Vinther; Oettinger, Thomas; Rosenkrands, Ida; Ravn, Pernille; Brock, Inger; Jacobsen, Susanne; Andersen, Peter [Reprint author]

CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark

SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. print.  
CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 22 Mar 2000  
Last Updated on STN: 3 Jan 2002

AB Culture filtrate from *Mycobacterium tuberculosis* contains protective antigens of relevance for the generation of a new antituberculosis vaccine. We have identified two previously uncharacterized *M. tuberculosis* proteins (TB7.3 and TB10.4) from the highly active low-mass fraction of culture filtrate. The molecules were characterized, mapped in a two-dimensional electrophoresis reference map of short-term culture filtrate, and compared with another recently identified low-mass protein, CFP10 (F. X. Berthet, P. B. Rasmussen, I.

Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203, 1998), and the well-described ESAT-6 antigen. Genetic analyses demonstrated that TB10.4 as well as CFP10 belongs to the ESAT-6 family of low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside this family. The proteins were expressed in Escherichia coli, and their immunogenicity was tested in cultures of peripheral blood mononuclear cells from human tuberculosis (TB) patients, *Mycobacterium bovis* BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and CFP10, were very strongly recognized and induced gamma interferon release at the same level (CFP10) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. CFP10 was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

=> e oettinger thomas/au

E1	5	OETTINGER T P/AU
E2	2	OETTINGER TH/AU
E3	22	--> OETTINGER THOMAS/AU
E4	7	OETTINGER THOMAS P/AU
E5	7	OETTINGER U/AU
E6	2	OETTINGER ULRICH/AU
E7	169	OETTINGER W/AU
E8	1	OETTINGER W H/AU
E9	1	OETTINGER W K/AU
E10	2	OETTINGER W K E/AU
E11	67	OETTINGER WILLI/AU
E12	3	OETTINGER WOLFGANG/AU

=> s e1-e4 and mycobact?

L6 24 ("OETTINGER T P"/AU OR "OETTINGER TH"/AU OR "OETTINGER THOMAS"/AU OR "OETTINGER THOMAS P"/AU) AND MYCOBACT?

=> dup rem 16

PROCESSING COMPLETED FOR L6

L7 13 DUP REM L6 (11 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 13 ANSWERS - CONTINUE? Y/(N):y

L7 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1  
 AN 2004:490265 CAPLUS  
 DN 141:52841

TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to *M. tuberculosis*, and use thereof as vaccines and in diagnosis

IN Andersen, Peter; Skjøt, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter

PA Den.

SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.  
 CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
PI US 2004115211	A1	20040617	US 2003-620246	20030715
US 6641814	B1	20031104	US 1998-50739	19980330
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI, CY

PRAI DK 1997-376 A 19970402  
 US 1997-44624P P 19970418

DK 1997-1277	A	19971110
US 1998-70488P	P	19980105
US 1998-50739	A2	19980330
DK 1998-1281	A	19981008
EP 1998-913536	A3	19980401

AB The present invention is based on the identification and characterization of a number of M. tuberculosis derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

L7 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2  
AN 2004:59568 CAPLUS  
DN 140:127185  
TI Antigens from **Mycobacterium** as vaccine and uses in tuberculosis diagnosis and treatment  
IN Andersen, Peter; Skjot, Rikke Louise Vinther; Okkels, Li Mei Meng; Brock, Inger; Oettinger, Thomas  
PA Den.  
SO U.S. Pat. Appl. Publ., 27 pp., Cont.-in-part of U.S. Ser. No. 804,980.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004013685	A1	20040122	US 2001-872505	20010601
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	WO 2001004151	A2	20010118	WO 2000-DK398	20000713
	WO 2001004151	A3	20010712		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003147897	A1	20030807	US 2001-804980	20010313
	US 6991797	B2	20060131		
PRAI	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1999-1020	A	19990713		
	US 1999-144011P	P	19990715		
	US 2000-615947	A2	20000713		
	WO 2000-DK398	A2	20000713		
	US 2001-804980	A2	20010313		
	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	US 1998-50739	A3	19980330		
	EP 1998-913536	A3	19980401		
	US 1999-289388	B2	19990412		
	US 2001-791171	A2	20010220		

AB The present invention is based on the identification and characterization of 3 antigens, including Rv2653c, Rv2654c and RD1-ORF5, from

**Mycobacterium tuberculosis.** The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing tuberculosis caused by virulent mycobacteria in an animal, including a human being. The invention related to treating tuberculosis using antigens isolated from **Mycobacterium tuberculosis**.

L7 ANSWER 3 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 3  
AN 2004:5335 BIOSIS  
DN PREV200400007544  
TI Nucleic acids fragments and polypeptide fragments derived from M.  
tuberculosis.  
AU Andersen, Peter [Inventor, Reprint Author]; Nielsen, Rikke [Inventor];  
Oettinger, Thomas [Inventor]; Rasmussen, Peter Birk [Inventor];  
Rosenkrands, Ida [Inventor]; Weldingh, Karin [Inventor]; Florio, Walter  
[Inventor]  
CS Bronshoj, Denmark  
ASSIGNEE: Statens Serum Institut, Copenhagen, Denmark  
PI US 6641814 20031104  
SO Official Gazette of the United States Patent and Trademark Office Patents,  
(Nov 4 2003) Vol. 1276, No. 1. <http://www.uspto.gov/web/menu/patdata.html>.  
e-file.  
ISSN: 0098-1133 (ISSN print).  
DT Patent  
LA English  
ED Entered STN: 17 Dec 2003  
Last Updated on STN: 17 Dec 2003  
AB The present invention is based on the identification and characterization of a number of M. tuberculosis derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L7 ANSWER 4 OF 13 USPATFULL on STN  
AN 2002:178550 USPATFULL  
TI Nucleic acid fragments and polypeptide fragments derived from M.  
tuberculosis  
IN Andersen, Peter, Bronshoj, DENMARK  
Nielsen, Rikke, Frederiksberg C, DENMARK  
Oettinger, Thomas, Hellerup, DENMARK  
Rasmussen, Peter Birk, Kobenhaven O, DENMARK  
Rosenkrands, Ida, Kobenhaven O, DENMARK  
Weldingh, Karin, Kobenhaven N, DENMARK  
Florio, Walter, Frederiksberg C, DENMARK  
PA STATENS SERUM INSTITUT (non-U.S. corporation)  
PI US 2002094336 A1 20020718  
AI US 2001-791171 A1 20010220 (9)  
RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING  
PRAI DK 1997-376 19970402  
DK 1997-1277 19971110  
US 1997-44624P 19970418 (60)  
US 1998-70488P 19980105 (60)  
DT Utility  
FS APPLICATION  
LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151  
CLMN Number of Claims: 53  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Page(s)  
LN.CNT 6134  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The present invention is based on the identification and

characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L7 ANSWER 5 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 4  
AN 2001:222123 BIOSIS  
DN PREV200100222123  
TI Diagnostic skin test for tuberculosis.  
AU Haslov, Kaare [Inventor]; Andersen, Ase Bengaard [Inventor];  
Oettinger, Thomas [Inventor]  
PI US 6120776 20000919  
SO Official Gazette of the United States Patent and Trademark Office Patents,  
(Sep. 19, 2000) Vol. 1238, No. 3. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DT Patent  
LA English  
ED Entered STN: 9 May 2001  
Last Updated on STN: 18 Feb 2002  
AB Diagnostic methods capable of discriminating between cell mediated immunologic responses due to on the one hand active tuberculosis caused by bacteria belonging to the tuberculosis complex (*Mycobacterium tuberculosis*, *Mycobacterium africanum* and *Mycobacterium bovis*) and on the other hand vaccination with an immunogenic agent conferring immunity to tuberculosis. A diagnostic kit is also provided, comprising a polypeptide (e.g. MPT64) capable of eliciting a delayed type hypersensitivity reaction (Dth) in animals with active tuberculosis, but not in animals vaccinated against TB with an immunogenic agent (e.g. *M. bovis* BCG strain: Danish 1331). Also provided are polypeptide fragments comprising a T-cell epitope of MPT64 as well as nucleic acid fragments encoding these polypeptide fragments.

L7 ANSWER 6 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 5  
AN 2000:104643 BIOSIS  
DN PREV200000104643  
TI Comparative evaluation of low-molecular-mass proteins from *Mycobacterium tuberculosis* identifies members of the ESAT-6 family as immunodominant T-cell antigens.  
AU Skjot, Rikke Louise Vinther; Oettinger, Thomas; Rosenkrands, Ida; Ravn, Pernille; Brock, Inger; Jacobsen, Susanne; Andersen, Peter [Reprint author]  
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark  
SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. print.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 22 Mar 2000  
Last Updated on STN: 3 Jan 2002  
AB Culture filtrate from *Mycobacterium tuberculosis* contains protective antigens of relevance for the generation of a new antituberculosis vaccine. We have identified two previously uncharacterized *M. tuberculosis* proteins (TB7.3 and TB10.4) from the highly active low-mass fraction of culture filtrate. The molecules were characterized, mapped in a two-dimensional electrophoresis reference map of short-term culture filtrate, and compared with another recently identified low-mass protein, CFP10 (F. X. Berthet, P. B. Rasmussen, I. Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203, 1998), and the well-described ESAT-6 antigen. Genetic analyses demonstrated that TB10.4 as well as CFP10 belongs to the ESAT-6 family of low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside

this family. The proteins were expressed in *Escherichia coli*, and their immunogenicity was tested in cultures of peripheral blood mononuclear cells from human tuberculosis (TB) patients, *Mycobacterium bovis* BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and CFP10, were very strongly recognized and induced gamma interferon release at the same level (CFP10) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. CFP10 was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

L7 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1998:684968 CAPLUS

DN 129:300060

TI Novel antigens of *Mycobacterium tuberculosis* culture filtrates

and the genes encoding and their diagnostic and prophylactic use

IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin;  
Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 264 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	AA	19981008	CA 1998-2285625	19980401
	AU 9868204	A1	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515359	T2	20010918	JP 1998-541074	19980401
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	CA 2319380	AA	19990520	CA 1998-2319380	19981008
	WO 9924577	A1	19990520	WO 1998-DK438	19981008
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1029053	A1	20000823	EP 1998-947412	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 504951	A	20010629	NZ 1998-504951	19981008
	AU 750173	B2	20020711	AU 1998-94338	19981008
	EP 1484405	A1	20041208	EP 2004-77071	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		

DK 1997-1277 A 19971110  
US 1998-70488P P 19980105  
EP 1998-913536 A3 19980401  
WO 1998-DK132 W 19980401  
EP 1998-947412 A3 19981008  
WO 1998-DK438 W 19981008

AB Culture filtrate antigens of *Mycobacterium tuberculosis* are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 6  
AN 1998:348514 BIOSIS  
DN PREV199800348514  
TI Delayed-type hypersensitivity responses to ESAT-6 and MPT64 from *Mycobacterium tuberculosis* in the guinea pig.  
AU Elhay, Martin J.; Oettinger, Thomas; Andersen, Peter [Reprint author]  
CS Dep. T.B. Immunol., Statens Serum Inst., Artillerivej 5, Copenhagen 2300, Denmark  
SO Infection and Immunity, (July, 1998) Vol. 66, No. 7, pp. 3454-3456. print.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 13 Aug 1998  
Last Updated on STN: 13 Aug 1998  
AB Two antigens from *Mycobacterium tuberculosis*, ESAT-6 and MPT64, elicited delayed-type hypersensitivity (DTH) skin responses in outbred guinea pigs infected with *M. tuberculosis* by the aerosol and intravenous routes but not those sensitized with *M. bovis* BCG or *M. avium*. The DTH epitope of ESAT-6 was mapped to the C terminus. Nonresponders to the individual antigens were found, but all animals responded to a combination of ESAT-6 and MPT64 or their respective minimal target peptides. Correspondingly, these molecules could form the basis of a new skin test for tuberculosis.

L7 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1996:632476 CAPLUS  
DN 125:325659  
TI Key epitopes on the ESAT-6 antigen recognized in mice during the recall of protective immunity to *Mycobacterium tuberculosis*  
AU Brandt, Lise; Oettinger, Thomas; Holm, Arne; Andersen, Aase B.; Andersen, Peter  
CS Bacterial Vaccine and Mycobacteria Dep., Royal Veterinary and Agricultural Univ., Copenhagen, Den.  
SO Journal of Immunology (1996), 157(8), 3527-3533  
CODEN: JOIMA3; ISSN: 0022-1767  
PB American Association of Immunologists  
DT Journal  
LA English  
AB The recall of long-lived immunity in a mouse model of tuberculosis (TB) is defined as an accelerated accumulation of reactive T cells in the target organs. The authors have recently identified antigen (Ag) 85B and a 6-kDa early secretory antigenic target, designated ESAT-6, as key antigenic targets recognized by these cells. Here, preferential recognition of the ESAT-6 Ag during the recall of immunity was shared by 5 of 6 genetically different strains of mice. Overlapping peptides spanning the sequence of ESAT-6 were used to map 2 T cell epitopes on this mol. One epitope recognized in the context of H-2b,d was located in the N-terminal part of the mol., whereas an epitope recognized in the context of H-2a,k covered

amino acids 51-60. Shorter versions of the N-terminal epitope allowed the precise definition of a 13-amino acid core sequence recognized in the context of H-2b. The peptide covering the N-terminal epitope was immunogenic, and a T cell response with the same fine specificity as that induced during TB infection was generated by immunization with the peptide in IFA. In the C57BL/6j strain, this single epitope was recognized by an exceedingly high frequency of splenic T cells (.apprx.1:1000), representing 25-35% of the total culture filtrate-reactive T cells recruited to the site of infection during the first phase of the recall response. These findings emphasize the relevance of this Ag in the immune response to TB and suggest that immunol. recognition in the first phase of infection is a highly restricted event dominated by a limited number of T cell clones.

L7 ANSWER 10 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 7

AN 1996:76919 BIOSIS

DN PREV199698649054

TI Evidence for occurrence of the ESAT-6 protein in **Mycobacterium** tuberculosis and virulent **Mycobacterium bovis** and for its absence in **Mycobacterium bovis** BCG.

AU Harboe, Morten [Reprint author]; Oettinger, Thomas; Wiker, Harald Gotten; Rosenkrands, Ida; Andersen, Peter

CS Inst. Immunol. Rheumatol., Univ. Oslo, N-0172 Oslo, Norway

SO Infection and Immunity, (1996) Vol. 64, No. 1, pp. 16-22.  
CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 27 Feb 1996  
Last Updated on STN: 27 Feb 1996

AB ESAT-6 is a secreted protein present in the short-term culture filtrate of **Mycobacterium** tuberculosis after growth on a synthetic Sauton medium. ESAT-6 has recently been demonstrated to induce strong T-cell responses in a mouse model of memory immunity after infection with *M. tuberculosis*. In Western blotting (immunoblotting), the monoclonal antibody HYB76-8, reacting with ESAT-6, gave a 6-kDa band in culture filtrates from *M. tuberculosis* and virulent **Mycobacterium bovis**. A distinct band in the 24-kDa region was observed in filtrates from four of eight substrains of *M. bovis* BCG that produced high levels of MPB64, while no band occurred in the 6-kDa region with any of these BCG substrains. Southern blotting and PCR experiments with genomic mycobacterial DNA showed the presence of the esat-6 gene in reference strains and clinical isolates of *V. tuberculosis* as well as in virulent *M. bovis*. The esat-6 gene could not be demonstrated in any of the eight substrains of *M. bovis* BCG tested by these techniques. Two gene deletions that distinguish *M. bovis* BCG from virulently *M. bovis* have thus now been demonstrated. Deletion of mpb64 affects four of the eight substrains tested; deletion of esat-6 affects all of them. The reaction of HYB76-8 at 26 kDa with four of the BCG substrains was demonstrated to result from cross-reactivity with MPB64. HYB76-8 was also shown to cross-react with the A, B, and C components of the antigen 85 complex and MPT51.

L7 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1995:498385 CAPLUS  
DN 122:260539

TI Diagnostic skin test for tuberculosis: a method able to distinguish infection from vaccination

IN Hasloev, Kaare; Andersen, Aase Bengaard; Oettinger, Thomas

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 85 pp.  
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
PI WO 9501440	A1	19950112	WO 1994-DK270	19940630
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DE, DK, DK,				

ES, FI, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD,  
MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, SK, TJ,  
TT, UA

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,  
BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9470686 A1 19950124 AU 1994-70686 19940630

AU 685133 B2 19980115

EP 749486 A1 19961227 EP 1994-919572 19940630

R: BE, CH, DE, ES, FR, GB, IT, LI

US 6120776 A 20000919 US 1996-569221 19960212

PRAI DK 1993-797 A 19930702

WO 1994-DK270 W 19940630

AB Diagnostic methods capable of discriminating between cell mediated immunol. responses due to on the one hand active tuberculosis caused by bacteria belonging to the tuberculosis complex (*Mycobacterium tuberculosis*, *Mycobacterium africanum* and *Mycobacterium bovis*) and on the other hand vaccination with an immunogenic agent conferring immunity to tuberculosis. A diagnostic kit is also provided, comprising a polypeptide (e.g. MPT64) capable of eliciting a delayed type hypersensitivity reaction in animals with active tuberculosis, but not in animals vaccinated against TB with an immunogenic agent (e.g. *M. bovis* BCG strain: Danish 1331). Also provided are polypeptide fragments comprising a T-cell epitope of MPT64 as well as nucleic acid fragments encoding these polypeptide fragments.

L7 ANSWER 12 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 8

AN 1996:21932 BIOSIS

DN PREV199698594067

TI Mapping of the delayed-type hypersensitivity-inducing epitope of secreted protein MPT64 from *Mycobacterium tuberculosis*.

AU Oettinger, Thomas [Reprint author]; Holm, Arne; Mtoni, Isaac M.;  
Andersen, Ase B.; Haslov, Kaare

CS Mycobacteria Dep., Div. Diagnostics, Statens Serum Institut, Artillerivej  
5, DK-2300 Copenhagen S, Denmark

SO Infection and Immunity, (1995) Vol. 63, No. 12, pp. 4613-4618.  
CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 12 Jan 1996

Last Updated on STN: 12 Jan 1996

AB The gene encoding the immunogenic protein MPT64 found in culture filtrates of *Mycobacterium tuberculosis* H37Rv was expressed in *Escherichia coli* K-12 and purified as a recombinant protein. The purified recombinant MPT64 elicited delayed-type hypersensitivity (DTH) in outbred guinea pigs sensitized with *Mycobacterium bovis* BCG Tokyo. The skin reactions were comparable to those obtained with native MPT64. No skin reactions were observed when either recombinant MPT64 or native MPT64 was used in guinea pigs sensitized with *M. bovis* BCG Danish 1331. Amino- and carboxy-terminal deletion mutants of MPT64 were purified as fusion proteins for the mapping of DTH-inducing epitopes on recombinant MPT64 by use of the guinea pig skin test model. The part of the molecule responsible for the biological activity was located at the carboxy-terminal end. Further studies with overlapping synthetic peptides have pinpointed the biological activity at a single DTH-inducing epitope consisting of 15 residues between amino acids Gly-173 and Ala-187. Screening by PCR of 56 clinical isolates of *M. tuberculosis* from Danish and Tanzanian patients demonstrated the presence of mpt64 in all of the strains. These results point to MPT64 as a possible candidate for a skin test reagent specific for diagnosis of human tuberculosis.

L7 ANSWER 13 OF 13 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 9

AN 1994:271662 BIOSIS

DN PREV199497284662

TI Cloning and B-cell-epitope mapping of MPT64 from *Mycobacterium tuberculosis* H37Rv.

AU Oettinger, Thomas [Reprint author]; Andersen, Ase B.

CS Mycobacteria Dep., Sector Biotechnol., Statens Serum Institut, Artillerivej

SO 5, DK-2300 Copenhagen S, Denmark  
Infection and Immunity, (1994) Vol. 62, No. 5, pp. 2058-2064.  
CODEN: INFIBR. ISSN: 0019-9567.

DT Article  
LA English  
OS EMBL-X75361  
ED Entered STN: 24 Jun 1994  
Last Updated on STN: 24 Jun 1994

AB The gene of the immunogenic protein MPT64 found in culture filtrates of *Mycobacterium tuberculosis* H37Rv was cloned and sequenced. A comparison showed mpt64 and the gene encoding MPB64 from *Mycobacterium bovis* BCG Tokyo to be identical except for one silent mutation. The regions encoding the promoter and the signal peptide were also well conserved for the two sequences. Southern blot experiments on genomic mycobacterial DNA showed the presence of mpt64 in the *M. tuberculosis* substrains H37Rv, H37Ra, and Erdman and in the *M. bovis* BCG substrains Tokyo, Moreau, and Russian, whereas the *M. bovis* BCG substrains Glaxo, Pasteur, Canadian, Tice, and Danish 1331 and *Mycobacterium leprae* lack the gene. Southern blot analyses revealed differences in the restriction enzyme patterns within the *M. tuberculosis* substrains as well as within the *M. bovis* BCG substrains, indicating either different chromosomal localization of mpt64 or that mutations have occurred at different locations on the chromosomes. N-terminal and C-terminal deletion mutants were constructed for the mapping of B-cell epitopes on MPT64 with five monoclonal antibodies, C24b1, C24b2, C24b3, L24b4, and L24b5. Western blot (immunoblot) analysis revealed that the murine antibodies bind to one linear and three conformational epitopes.

=> e rasmussen peter b/au

E1 32 RASMUSSEN PETER A/AU  
E2 1 RASMUSSEN PETER ANDREAS/AU  
E3 1 --> RASMUSSEN PETER B/AU  
E4 48 RASMUSSEN PETER BIRK/AU  
E5 2 RASMUSSEN PETER BOYEN/AU  
E6 1 RASMUSSEN PETER C/AU  
E7 1 RASMUSSEN PETER CHR/AU  
E8 6 RASMUSSEN PETER CHRISTIAN/AU  
E9 3 RASMUSSEN PETER D/AU  
E10 2 RASMUSSEN PETER F/AU  
E11 1 RASMUSSEN PETER G/AU  
E12 1 RASMUSSEN PETER HAARGAARD/AU

=> s e3-e4 and mycobact?

L8 30 ("RASMUSSEN PETER B"/AU OR "RASMUSSEN PETER BIRK"/AU) AND MYCOBA  
CT?

=> dup rem 18

PROCESSING COMPLETED FOR L8

L9 21 DUP REM L8 (9 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 21 ANSWERS - CONTINUE? Y/ (N) :y

L9 ANSWER 1 OF 21 USPATFULL on STN  
AN 2006:9617 USPATFULL  
TI Novel methods for therapeutic vaccination  
IN Steinaa, Lucilla, Copenhagen V, DENMARK  
Mouritsen, Soren, Birkerod, DENMARK  
Gautam, Anand, Horsholm, DENMARK  
Dalum, Iben, Horsholm, DENMARK  
Hanning, Jesper, Birkerod, DENMARK  
Leach, Dana, Copenhagen O, DENMARK  
Nielsen, Klaus Gregorius, Soborg, DENMARK  
Karlsson, Gunilla, Copenhagen O, DENMARK  
Rasmussen, Peter Birk, Frederiksberg, DENMARK  
PA PHARMEXA A/S, Horsholm, DENMARK (non-U.S. corporation)

PI US 2006008465 A1 20060112  
AI US 2005-202516 A1 20050811 (11)  
RLI Division of Ser. No. US 2001-806703, filed on 30 Apr 2001, PENDING A 371  
of International Ser. No. WO 1999-DK525, filed on 5 Oct 1999  
PRAI DK 1998-1261 19981005  
US 1998-105011P 19981020 (60)  
DT Utility  
FS APPLICATION  
LREP BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747,  
US  
CLMN Number of Claims: 23  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Page(s)  
LN.CNT 5986

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. PSM, Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by using live attenuated vaccines or nucleic acid vaccination. The invention furthermore provides immunogenic analogues of PSM, Her2 and FGF8b, as well as nucleic acid molecules encoding these analogues. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogues of weak or non-immunogenic antigens.

L9 ANSWER 2 OF 21 USPATFULL on STN  
AN 2006:49294 USPATFULL  
TI Methods for therapeutic vaccination  
IN Steinaa, Lucilla, Copenhagen, DENMARK  
Mouritsen, S.o slashed.ren, Birker.o slashed.d, DENMARK  
Gautam, Anand, H.o slashed.rsholm, DENMARK  
Dalum, Iben, H.o slashed.rsholm, DENMARK  
Hanning, Jesper, Birker.o slashed.d, DENMARK  
Leach, Dana, Copenhagen .O slashed., DENMARK  
Nielsen, Klaus Gregorius, S.o slashed.borg, DENMARK  
Karlsson, Gunilla, Copenhagen .O slashed., DENMARK  
Rasmussen, Peter Birk, Frederiksberg, DENMARK

PA Pharmexa A/s, Horsholm, DENMARK (non-U.S. corporation)  
PI US 7005498 B1 20060228  
WO 2000020027 20000413  
AI US 2001-806703 19991005 (9)  
WO 1999-DK525 19991005  
20010430 PCT 371 date

PRAI DK 1998-1261 19981005  
US 2001-105011P 19981020 (60)

DT Utility  
FS GRANTED

EXNAM Primary Examiner: Chan, Christina; Assistant Examiner: DiBrino, Marianne  
LREP Birch, Stewart, Kolasch & Birch, LLP  
CLMN Number of Claims: 5  
ECL Exemplary Claim: 1  
DRWN 7 Drawing Figure(s); 6 Drawing Page(s)  
LN.CNT 6182

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is disclosed for inducing cell-mediated immunity against cellular antigens. More specifically, the invention provides for a method for inducing cytotoxic T-lymphocyte immunity against weak antigens, notably self-proteins. The method entails that antigen presenting cells are induced to present at least one CTL epitope of the weak antigen and at the same time presenting at least one foreign T-helper lymphocyte epitope. In a preferred embodiment, the antigen is a cancer specific antigen, e.g. PSM, Her2, or FGF8b. The method can be exercised by using traditional polypeptide vaccination, but also by

using live attenuated vaccines or nucleic acid vaccination. The invention furthermore provides immunogenic analogues of PSM, Her2 and FGF8b, as well as nucleic acid molecules encoding these analogues. Also vectors and transformed cells are disclosed. The invention also provides for a method for identification of immunogenic analogues of weak or non-immunogenic antigens.

L9 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2005:409557 CAPLUS

DN 142:442339

TI Method for down-regulation of VEGF using immunogenic VEGF analogs in disease treatment

IN Rasmussen, Peter Birk; Dal Degan, Florence; Renard, Valery;  
Klysner, Steen; Volck, Birgitte

PA Pharmexa A/S, Den.

SO PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005042575	A2	20050512	WO 2004-DK741	20041028
WO 2005042575	A3	20050623		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRAI DK 2003-1612 A 20031030  
US 2003-516596P P 20031031

AB The present invention provides for novel immunogenic variants of VEGF (vascular endothelial growth factor) which are useful in active specific immunotherapy against diseases that are characterized by overexpression of VEGF. The invention also relates to methods of treating such diseases (for instance cancer) as well as to various tools in mol. biol. that assist in the provision of the immunogenic variants.

L9 ANSWER 4 OF 21 USPATFULL on STN

AN 2005:208471 USPATFULL

TI Novel application of vaccination against TNF-alpha

IN Pedersen, Hans Rudolf, Valby, DENMARK

Ebert, Bjarke, Valby, DENMARK

Pedersen, Louise Henriette, Valby, DENMARK

Rasmussen, Peter Birk, Horsholm, DENMARK

PI US 2005180947 A1 20050818

AI US 2004-939107 A1 20040910 (10)

RLI Continuation-in-part of Ser. No. WO 2003-DK147, filed on 11 Mar 2003,  
UNKNOWN

PRAI DK 2002-368 20020311

US 2002-363128P 20020311 (60)

DT Utility

FS APPLICATION

LREP FROMMER LAWRENCE & HAUG, 745 FIFTH AVENUE- 10TH FL., NEW YORK, NY,  
10151, US

CLMN Number of Claims: 8

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 5591

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to novel medical applications of down-regulation of tumour necrosis factor  $\alpha$  (TNF- $\alpha$ ) activity, especially novel applications of active immunization against

TNF-a in order to reduce or alleviate pain. In particular, the present invention discloses novel methods for treating or ameliorating neuropathic pain.

L9 ANSWER 5 OF 21 USPATFULL on STN  
AN 2005:188836 USPATFULL  
TI Novel method for down-regulation of amyloid  
IN Rasmussen, Peter Birk, Horsholm, DENMARK  
Jensen, Martin Roland, Horsholm, DENMARK  
Nielsen, Klaus Gregorius, Horsholm, DENMARK  
Koefoed, Peter, Horsholm, DENMARK  
Degan, Florence Dal, Horsholm, DENMARK  
PI US 2005163744 A1 20050728  
AI US 2004-783317 A1 20040220 (10)  
RLI Continuation-in-part of Ser. No. WO 2002-DK547, filed on 20 Aug 2002,  
UNKNOWN  
PRAI DK 2001-1231 20010820  
DK 2002-558 20020416  
US 2001-337543P 20011022 (60)  
US 2002-373027P 20020416 (60)  
DT Utility  
FS APPLICATION  
LREP FROMMER LAWRENCE & HAUG, 745 FIFTH AVENUE- 10TH FL., NEW YORK, NY,  
10151, US  
CLMN Number of Claims: 51  
ECL Exemplary Claim: 1  
DRWN 2 Drawing Page(s)  
LN.CNT 3623  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB Disclosed are novel methods for combatting diseases characterized by deposition of amyloid. The methods generally rely on immunization against amyloid precursor protein (APP) or beta amyloid (A $\beta$ ). Immunization is preferably effected by administration of analogues of autologous APP or A $\beta$ , said analogues being capable of inducing antibody production against the autologous amyloidogenic polypeptides. Especially preferred as an immunogen is autologous A $\beta$  which has been modified by introduction of one single or a few foreign, immunodominant and promiscuous T-cell epitopes. Also disclosed are nucleic acid vaccination against APP or A $\beta$  and vaccination using live vaccines as well as methods and means useful for the vaccination. Such methods and means include methods for the preparation of analogues and pharmaceutical formulations, as well as nucleic acid fragments, vectors, transformed cells, polypeptides and pharmaceutical formulations.

L9 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1  
AN 2004:490265 CAPLUS  
DN 141:52841  
TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to M. tuberculosis, and use thereof as vaccines and in diagnosis  
IN Andersen, Peter; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter  
Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter  
PA Den.  
SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004115211	A1	20040617	US 2003-620246	20030715
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		

DK	1997-1277	A	19971110
US	1998-70488P	P	19980105
US	1998-50739	A2	19980330
DK	1998-1281	A	19981008
EP	1998-913536	A3	19980401

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

L9 ANSWER 7 OF 21 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 2

AN 2004:5335 BIOSIS

DN PREV200400007544

TI Nucleic acids fragments and polypeptide fragments derived from *M. tuberculosis*.

AU Andersen, Peter [Inventor, Reprint Author]; Nielsen, Rikke [Inventor]; Oettinger, Thomas [Inventor]; **Rasmussen, Peter Birk** [Inventor]; Rosenkrands, Ida [Inventor]; Weldingh, Karin [Inventor]; Florio, Walter [Inventor]

CS Bronshoj, Denmark

ASSIGNEE: Statens Serum Institut, Copenhagen, Denmark

PI US 6641814 20031104

SO Official Gazette of the United States Patent and Trademark Office Patents, (Nov 4 2003) Vol. 1276, No. 1. <http://www.uspto.gov/web/menu/patdata.html>. e-file.

ISSN: 0098-1133 (ISSN print).

DT Patent

LA English

ED Entered STN: 17 Dec 2003

Last Updated on STN: 17 Dec 2003

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L9 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

AN 2003:696302 CAPLUS

DN 139:229237

TI Protein and DNA sequences of antigens from *Mycobacterium* and uses in tuberculosis diagnosis and treatment

IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Vegerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; **Rasmussen, Peter Birk**

PA Statens Serum Institut, Den.

SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.

CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6982085	B2	20060103		
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401

EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI DK 1997-376	A	19970402		
US 1997-44624P	P	19970418		
DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
US 1998-50739	A2	19980330		
DK 1998-1281	A	19981008		
US 2001-791171	B2	20010220		
US 2002-60428	A2	20020129		
EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from **Mycobacterium tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing tuberculosis caused by virulent mycobacteria, e.g. by **Mycobacterium tuberculosis**, **Mycobacterium africanum** or **Mycobacterium bovis**, in an animal, including a human being. The invention related to treating tuberculosis using antigens isolated from **Mycobacterium tuberculosis**.

L9 ANSWER 9 OF 21 USPATFULL on STN

AN 2003:225306 USPATFULL

TI Novel method for down-regulation of amyloid  
IN Rasmussen, Peter Birk, Horsholm, DENMARK  
Jensen, Martin Roland, Horsholm, DENMARK  
Nielsen, Klaus Gregorius, Horsholm, DENMARK  
Koefoed, Peter, Horsholm, DENMARK  
Degan, Florence Dal, Horsholm, DENMARK

PI US 2003157117 A1 20030821

AI US 2002-223809 A1 20020820 (10)

PRAI DK 2001-1231 20010820

DK 2002-58 20020416

US 2001-337543P 20011022 (60)

US 2002-373027P 20020416 (60)

DT Utility

FS APPLICATION

LREP FROMMER LAWRENCE & HAUG, 745 FIFTH AVENUE- 10TH FL., NEW YORK, NY, 10151

CLMN Number of Claims: 42

ECL Exemplary Claim: 1

DRWN 2 Drawing Page(s)

LN.CNT 3681

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are novel methods for combatting diseases characterized by deposition of amyloid. The methods generally rely on immunization against amyloid precursor protein (APP) or beta amyloid (A $\beta$ ). Immunization is preferably effected by administration of analogues of autologous APP or A $\beta$ , said analogues being capable of inducing antibody production against the autologous amyloidogenic polypeptides. Especially preferred as an immunogen is autologous A $\beta$  which has been modified by introduction of one single or a few foreign, immunodominant and promiscuous T-cell epitopes. Also disclosed are nucleic acid vaccination against APP or A $\beta$  and vaccination using live vaccines as well as methods and means useful for the vaccination. Such methods and means include methods for the preparation of analogues and pharmaceutical formulations, as well as nucleic acid fragments, vectors, transformed cells, polypeptides and pharmaceutical formulations.

L9 ANSWER 10 OF 21 USPATFULL on STN

AN 2003:134810 USPATFULL

TI Polynucleotide functionally coding for the LHP protein from **Mycobacterium tuberculosis**, its biologically active derivative fragments, as well as methods using the same

IN Gicquel, Brigitte, Paris, FRANCE  
Berthet, Francois-Xavier, Paris, FRANCE  
Anderson, Peter, Bronshoj, DENMARK  
Rasmussen, Peter Birk, Bergsgade, DENMARK

PA INSTITUT PASTEUR, Paris Cedex, FRANCE (non-U.S. corporation)

PI US 2003092899 A1 20030515

AI US 2002-140045 A1 20020508 (10)

RLI Division of Ser. No. US 1998-116492, filed on 16 Jul 1998, GRANTED, Pat.  
No. US 6436409

PRAI US 1997-52631P 19970716 (60)

DT Utility

FS APPLICATION

LREP OBLON SPIVAK MCCLELLAND MAIER & NEUSTADT PC, FOURTH FLOOR, 1755  
JEFFERSON DAVIS HIGHWAY, ARLINGTON, VA, 22202

CLMN Number of Claims: 55

ECL Exemplary Claim: 1

DRWN 14 Drawing Page(s)

LN.CNT 2572

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to a polynucleotide carrying an open reading frame coding for an antigenic polypeptide from **Mycobacterium tuberculosis**, named lhp, which is placed under the control of its own regulation signals which are functional in **mycobacteria**, specially in **mycobacteria** belonging to the **Mycobacterium tuberculosis** complex and also in fast growing **mycobacteria** such as **Mycobacterium smegmatis**. The invention is also directed to the polypeptide LHP encoded by lhp and most preferably to suitable antigenic portions of LHP as well as to oligomeric polypeptides containing more than one unit of LHP or an antigenic portion of LHP. The invention concerns also immunogenic and vaccine compositions containing a polypeptide or an oligomeric polypeptide such as defined above, as well as antibodies directed specifically against such polypeptides that are useful as diagnostic reagents. In another embodiment, the present invention is directed to a polynucleotide carrying the natural regulation signals of lhp which is useful in order to express heterologous proteins in **mycobacteria**. Finally, the present invention is directed to oligonucleotides comprising at least 12 consecutive nucleotides from the regulation sequence of lhp which are useful as reagents for detecting the presence of **Mycobacterium tuberculosis** in a biological sample.

L9 ANSWER 11 OF 21 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 4

AN 2002:512984 BIOSIS

DN PREV200200512984

TI Polynucleotide functionally coding for the LHP protein from **Mycobacterium tuberculosis**, its biologically active derivative fragments, as well as methods using the same.

AU Gicquel, Brigitte [Inventor, Reprint author]; Berthet, Francois-Xavier [Inventor]; Andersen, Peter [Inventor]; Rasmussen, Peter Birk [Inventor]

CS Paris, France  
ASSIGNEE: Institut Pasteur, Paris, France

PI US 6436409 20020820

SO Official Gazette of the United States Patent and Trademark Office Patents, (Aug. 20, 2002) Vol. 1261, No. 3. <http://www.uspto.gov/web/menu/patdata.html>. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.

DT Patent

LA English

ED Entered STN: 2 Oct 2002  
Last Updated on STN: 2 Oct 2002

AB The present invention is directed to a polynucleotide carrying an open reading frame coding for an antigenic polypeptide from **Mycobacterium tuberculosis**, named lhp, which is placed under the control of its own regulation signals which are functional in **mycobacteria**, specially in **mycobacteria** belonging to the **Mycobacterium tuberculosis** complex and also in fast growing **mycobacteria** such as **Mycobacterium smegmatis**. The

invention is also directed to the polypeptide LHP encoded by lhp and most preferably to suitable antigenic portions of LHP as well as to oligomeric polypeptides containing more than one unit of LHP or an antigenic portion of LHP. The invention concerns also immunogenic and vaccine compositions containing a polypeptide or an oligomeric polypeptide such as defined above, as well as antibodies directed specifically against such polypeptides that are useful as diagnostic reagents. In another embodiment, the present invention is directed to a polynucleotide carrying the natural regulation signals of lhp which is useful in order to express heterologous proteins in mycobacteria. Finally, the present invention is directed to oligonucleotides comprising at least 12 consecutive nucleotides from the regulation sequence of lhp which are useful as reagents for detecting the presence of **Mycobacterium tuberculosis** in a biological sample.

L9 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5  
AN 2002:906996 CAPLUS  
DN 138:13499  
TI Hybrids of M. tuberculosis antigens used as vaccines  
IN Andersen, Peter; Olsen, Anja Weinreich; Skjot, Rikke Louise Vinther;  
Rasmussen, Peter Birk  
PA Den.  
SO U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S. Ser. No. 246,191,  
abandoned.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002176867	A1	20021128	US 2001-805427	20010313
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-246191	B2	19981230		
	DK 1997-376	A	19970402		
	EP 1998-913536	A3	19980401		

AB The invention discloses fusion proteins consisting of T cell epitopes derived from the immunodominant antigens ESAT-6 and Ag85B from **Mycobacterium tuberculosis** or homologs thereof, and a tuberculosis vaccine based on the fusion proteins, which induces efficient immunol. memory. It is preferred that the sequences of the first and second T cell epitopes each have a sequence identity of at least 70% with the natively occurring sequence in the proteins from which they are derived. In the most preferred embodiment, the fusion polypeptide comprises ESAT-6 fused to Ag85B wherein ESAT-6 is fused to the C terminus of Ag85B. In one embodiment, there are nitric oxide linkers introduced between the 2 amino acid sequences constituting the parent polypeptide fragments.

L9 ANSWER 13 OF 21 USPATFULL on STN  
AN 2002:329478 USPATFULL  
TI Novel method for down-regulation of amyloid  
IN Jensen, Martin Roland, Holte, DENMARK  
Rasmussen, Peter Birk, Frederiksberg, DENMARK  
Nielsen, Klaus Gregorius, Soborg, DENMARK  
PI US 2002187157 A1 20021212  
AI US 2001-785215 A1 20010220 (9)  
PRAI PA 2000-200000265 20000221  
US 2000-186295P 20000301 (60)  
DT Utility  
FS APPLICATION  
LREP BIRCH STEWART KOLASCH & BIRCH, PO BOX 747, FALLS CHURCH, VA, 22040-0747  
CLMN Number of Claims: 58  
ECL Exemplary Claim: 1  
DRWN 1 Drawing Page(s)

LN.CNT 3272

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method for in vivo down-regulation of amyloid protein in an animal, including a human being, the method comprising effecting presentation to the animal's immune system of an immunogenically effective amount of at least one amyloidogenic polypeptide or subsequence thereof which has been formulated so that immunization of the animal with the amyloidogenic polypeptide or subsequence thereof induces production of antibodies against the amyloidogenic polypeptide, and/or at least one analogue of the amyloidogenic polypeptide wherein is introduced at least one modification in the amino acid sequence of the amyloidogenic polypeptide which has as a result the immunization of the animal with the analogue induces production of antibodies against the amyloidogenic polypeptide.

L9 ANSWER 14 OF 21 USPATFULL on STN

AN 2002:178550 USPATFULL

TI Nucleic acid fragments and polypeptide fragments derived from M. tuberculosis

IN Andersen, Peter, Bronshoj, DENMARK  
Nielsen, Rikke, Frederiksberg C, DENMARK  
Oettinger, Thomas, Hellerup, DENMARK

Rasmussen, Peter Birk, Kobenhavn O, DENMARK

Rosenkrands, Ida, Kobenhavn O, DENMARK

Weldingh, Karin, Kobenhavn N, DENMARK

Florio, Walter, Frederiksberg C, DENMARK

PA STATENS SERUM INSTITUT (non-U.S. corporation)

PI US 2002094336 A1 20020718

AI US 2001-791171 A1 20010220 (9)

RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING

PRAI DK 1997-376 19970402

DK 1997-1277 19971110

US 1997-44624P 19970418 (60)

US 1998-70488P 19980105 (60)

DT Utility

FS APPLICATION

LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151

CLMN Number of Claims: 53

ECL Exemplary Claim: 1

DRWN 6 Drawing Page(s)

LN.CNT 6134

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is based on the identification and characterization of a number of M. tuberculosis derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L9 ANSWER 15 OF 21 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 6

AN 2001:302988 BIOSIS

DN PREV200100302988

TI Protection of mice with a tuberculosis subunit vaccine based on a fusion protein of antigen 85B and ESAT-6.

AU Olsen, Anja Weinreich; van Pinxteren, Laurens A. H.; Okkels, Limei Meng;  
Rasmussen, Peter Birk; Andersen, Peter [Reprint author]

CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5,  
DK-2300, Copenhagen S, Denmark

pa@ssi.dk

SO Infection and Immunity, (May, 2001) Vol. 69, No. 5, pp. 2773-2778. print.  
CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 27 Jun 2001

AB Last Updated on STN: 19 Feb 2002

In this study, we investigated the potential of a tuberculosis subunit vaccine based on fusion proteins of the immunodominant antigens ESAT-6 and antigen 85B. When the fusion proteins were administered to mice in the adjuvant combination dimethyl dioctadecylammonium bromide-monophosphoryl lipid A, a strong dose-dependent immune response was induced to both single components as well as to the fusion proteins. The immune response induced was accompanied by high levels of protective immunity and reached the level of *Mycobacterium bovis* BCG-induced protection over a broad dose range. The vaccine induced efficient immunological memory, which remained stable 30 weeks postvaccination.

L9 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1999:77692 CAPLUS

DN 130:165432

TI The antigenic protein LHP of *Mycobacterium tuberculosis* and the lhp gene encoding it and their diagnostic and prophylactic uses  
IN Gicquel, Brigitte; Berthet, Francois-Xavier; Andersen, Peter;  
Rasmussen, Peter Birk

PA Institut Pasteur, Fr.; Statens Serum Institut

SO PCT Int. Appl., 88 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9904005	A1	19990128	WO 1998-IB1091	19980716
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2296419	AA	19990128	CA 1998-2296419	19980716
	AU 9881238	A1	19990210	AU 1998-81238	19980716
	EP 1003870	A1	20000531	EP 1998-930967	19980716
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6436409	B1	20020820	US 1998-116492	19980716
	US 2003092899	A1	20030515	US 2002-140045	20020508
PRAI	US 1997-52631P	P	19970716		
	US 1998-116492	A3	19980716		
	WO 1998-IB1091	W	19980716		

AB The *Mycobacterium tuberculosis* gene encoding the antigenic protein LHP that is homologous to the L45 antigen of *M. bovis*, is cloned and characterized. The gene can be expressed from its own promoter in slow-growing (*M. tuberculosis* group) and fast-growing (*M. smegmatis*) mycobacteria. The LHP gene product, and antigenic peptides derived from it, can be manufactured for use in vaccines and to raise reagent antibodies for diagnostic use. The promoter of the lhp gene may be of use in the expression of foreign genes in *Mycobacteria*. Oligonucleotides derived from the promoter region may be useful as probes or primers in the detection of *M. tuberculosis* in a biol. sample. Anal. of the promoters driving expression of the closely linked lhp and orf1C genes of *M. tuberculosis* established that they form an operon. Use of the promoter to drive expression of a reporter gene in *M. smegmatis* is demonstrated. The protein is abundant in short-term (7 day) culture filtrates of *M. tuberculosis*.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 21 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 7

AN 2000:34114 BIOSIS

DN PREV200000034114

TI Differential T-cell recognition of native and recombinant

AU **Mycobacterium tuberculosis GroES.**  
 Rosenkrands, Ida; Weldingh, Karin; Ravn, Pernille; Brandt, Lise; Hojrup, Peter; **Rasmussen, Peter Birk**; Coates, Anthony R.; Singh, Mahavir; Mascagni, Paolo; Andersen, Peter [Reprint author]  
 CS Department of TB Immunology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen S, Denmark  
 SO Infection and Immunity, (Nov., 1999) Vol. 67, No. 11, pp. 5552-5558.  
 print.  
 CODEN: INFIBR. ISSN: 0019-9567.  
 DT Article  
 LA English  
 ED Entered STN: 19 Jan 2000  
 Last Updated on STN: 31 Dec 2001  
 AB **Mycobacterium tuberculosis GroES** was purified from culture filtrate, and its identity was confirmed by immunoblot analysis and N-terminal sequencing. Comparing the immunological recognition of native and recombinant GroES, we found that whereas native GroES elicited a strong proliferative response and release of gamma interferon-gamma by peripheral blood mononuclear cells from healthy tuberculin reactors, the recombinant protein failed to do so. The same difference in immunological recognition was observed in a mouse model of TB infection. Both the native and recombinant preparations were recognized by mice immunized with the recombinant protein. Biochemical characterization including sodium dodecyl sulfate-polyacrylamide gel electrophoresis, two-dimensional electrophoresis, and mass spectrometry analysis of both proteins demonstrated no differences between the native and recombinant forms of GroES except for the eight additional N-terminal amino acids derived from the fusion partner inrecombinant GroES. The recombinant fusion protein, still tagged with the maltose binding protein, was recognized by T cells isolated from TB-infected mice if mixed with culture filtrate before affinity purification on an amylose column. The maltose binding protein treated in the same manner as a control preparation was not recognized. Based on the data presented, we suggest that the association of biologically active molecules from culture filtrate with the chaperone GroES may be responsible for the observed T-cell recognition of the native preparation.

L9 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 1998:684968 CAPLUS  
 DN 129:300060  
 TI Novel antigens of **Mycobacterium tuberculosis** culture filtrates and the genes encoding and their diagnostic and prophylactic use  
 IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; **Rasmussen, Peter Birk**; Oettinger, Thomas; Florio, Walter  
 PA Statens Serum Institut, Den.  
 SO PCT Int. Appl., 264 pp.  
 CODEN: PIXXD2

DT Patent  
 LA English  
 FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	AA	19981008	CA 1998-2285625	19980401
	AU 9868204	A1	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515359	T2	20010918	JP 1998-541074	19980401
	EP 1449922	A2	20040825	EP 2004-76605	19980401

EP 1449922 A3 20041117  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI, CY  
 CA 2319380 AA 19990520 CA 1998-2319380 19981008  
 WO 9924577 A1 19990520 WO 1998-DK438 19981008  
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,  
 DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,  
 KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,  
 MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,  
 TT, UA, UG, US, UZ, VN, YU, ZW  
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 1029053 A1 20000823 EP 1998-947412 19981008  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 NZ 504951 A 20010629 NZ 1998-504951 19981008  
 AU 750173 B2 20020711 AU 1998-94338 19981008  
 EP 1484405 A1 20041208 EP 2004-77071 19981008  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI, CY  
 PRAI DK 1997-376 A 19970402  
 US 1997-44624P P 19970418  
 DK 1997-1277 A 19971110  
 US 1998-70488P P 19980105  
 EP 1998-913536 A3 19980401  
 WO 1998-DK132 W 19980401  
 EP 1998-947412 A3 19981008  
 WO 1998-DK438 W 19981008

AB Culture filtrate antigens of *Mycobacterium tuberculosis* are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 19 OF 21 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
 STN DUPLICATE 8  
 AN 1998:393332 BIOSIS  
 DN PREV199800393332  
 TI Two-dimensional electrophoresis for analysis of *Mycobacterium tuberculosis* culture filtrate and purification and characterization of six novel proteins.  
 AU Weldingh, Karin; Rosenkrands, Ida; Jacobsen, Susanne; Rasmussen, Peter Birk; Elhay, Martin J.; Andersen, Peter [Reprint author]  
 CS Dep. TB Immunol., Statens Serum Inst., Artillerivej 5, DK-2300 Copenhagen, Denmark  
 SO Infection and Immunity, (Aug., 1998) Vol. 66, No. 8, pp. 3492-3500. print.  
 CODEN: INFIBR. ISSN: 0019-9567.  
 DT Article  
 LA English  
 ED Entered STN: 10 Sep 1998  
 Last Updated on STN: 10 Sep 1998  
 AB Culture filtrate from *Mycobacterium tuberculosis* contains molecules which promote high levels of protective immunity in animal models of subunit vaccination against tuberculosis. We have used two-dimensional electrophoresis for analysis and purification of six novel *M. tuberculosis* culture filtrate proteins (CFPs): CFP17, CFP20, CFP21, CFP22, CFP25, and CFP28. The proteins were tested for recognition by *M. tuberculosis*-reactive memory cells from different strains of inbred mice and for their capacity to induce a skin test response in *M. tuberculosis*-infected guinea pigs. CFP17, CFP20, CFP21 and CFP25 induced both a high gamma interferon release and a strong delayed-type

hypersensitivity response, and CFP21 was broadly recognized by different strains of inbred mice. N-terminal sequences were obtained for the six proteins, and the corresponding genes were identified in the Sanger M. tuberculosis genome database. In parallel we established a two-dimensional electrophoresis reference map of short-term culture filtrate components and mapped novel proteins as well as already-known CFP.

L9 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1998:753589 CAPLUS  
DN 130:120272  
TI A *Mycobacterium* tuberculosis operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10)  
AU Berthet, Francois-Xavier; Rasmussen, Peter Birk; Rosenkrands, Ida; Andersen, Peter; Gicquel, Brigitte  
CS Unite de Genetique Mycobacterienne, Institut Pasteur, Paris, 75724, Fr.  
SO Microbiology (Reading, United Kingdom) (1998), 144(11), 3195-3203  
CODEN: MROBEO; ISSN: 1350-0872  
PB Society for General Microbiology  
DT Journal  
LA English  
AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by *Mycobacterium* tuberculosis. Its corresponding gene (esat-6) is located in RD1, a 10kb DNA region deleted in the attenuated tuberculosis vaccine strain *Mycobacterium bovis* BCG. The promoter region of *M. tuberculosis* esat-6 was cloned and characterized. A new gene, designated lhp and cotranscribed with esat-6, was identified. Moreover, computer searches in the *M. tuberculosis* genome identified 13 genes related to the lhp/esat-6 operon, defining a novel gene family. The transcription initiation sites of the lhp/esat-6 operon were mapped using *M. tuberculosis* RNA. The corresponding promoter signals were not recognized in *Mycobacterium smegmatis*, in which transcription of lhp/esat-6 is initiated at different locations. The *M. tuberculosis* lhp gene product was identified as CFP-10, a low-mol.-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in *M. tuberculosis* and that both code for small exported proteins.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 21 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 9  
AN 1998:304925 BIOSIS  
DN PREV199800304925  
TI Identification and characterization of a 29-kilodalton protein from *Mycobacterium* tuberculosis culture filtrate recognized by mouse memory effector cells.  
AU Rosenkrands, Ida; Rasmussen, Peter Birk; Carnio, Markus; Jacobsen, Susanne; Theisen, Michael; Andersen, Peter [Reprint author]  
CS Dep. TB Immunol., Statens Serum Inst., 5 Artillerivej, DK-2300 Copenhagen S, Denmark  
SO Infection and Immunity, (June, 1998) Vol. 66, No. 6, pp. 2728-2735. print.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
OS Genbank-Y12820; EMBL-Y12820; DDBJ-Y12820  
ED Entered STN: 15 Jul 1998  
Last Updated on STN: 15 Jul 1998  
AB Culture filtrate proteins from *Mycobacterium* tuberculosis induce protective immunity in various animal models of tuberculosis. Two molecular mass regions (6 to 10 kDa and 24 to 36 kDa) of short-term culture filtrate are preferentially recognized by Th1 cells in animal models as well as by patients with minimal disease. In the present study, the 24- to 36-kDa region has been studied, and the T-cell reactivity has been mapped in detail. Monoclonal antibodies were generated, and one monoclonal antibody, HYB 71-2, with reactivity against a 29-kDa antigen located in the highly reactive region below the antigen 85 complex was selected. The 29-kDa antigen (CFP29) was purified from *M. tuberculosis*

short-term culture filtrate by thiophilic adsorption chromatography, anion-exchange chromatography, and gel filtration. In its native form, CFP29 forms a polymer with a high molecular mass. CFP29 was mapped in two-dimensional electrophoresis gels as three distinct spots just below the antigen 85 complex component MPT59. CFP29 is present in both culture filtrate and the membrane fraction from *M. tuberculosis*, suggesting that this antigen is released from the envelope to culture filtrate during growth. Determination of the N-terminal amino acid sequence allowed cloning and sequencing of the cfp29 gene. The nucleotide sequence showed 62% identity to the bacteriocin Linocin from *Brevibacterium linens*. Purified recombinant histidine-tagged CFP29 and native CFP29 had similar T-cell stimulatory properties, and they both elicited the release of high levels of gamma interferon from mouse memory effector cells isolated during the recall of protective immunity to tuberculosis. Interspecies analysis by immunoblotting and PCR demonstrated that CFP29 is widely distributed in mycobacterial species.

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E1 1 ROSENKRANDS G/AU  
E2 73 ROSENKRANDS I/AU  
E3 68 --> ROSENKRANDS IDA/AU  
E4 1 ROSENKRANDS JOHANNES W/AU  
E5 2 ROSENKRANDS NIELS PETER/AU  
E6 1 ROSENKRANDS P/AU  
E7 1 ROSENKRANDS T/AU  
E8 5 ROSENKRANDS V/AU  
E9 1 ROSENKRANK MAGNUS/AU  
E10 1 ROSENKRANS/AU  
E11 1 ROSENKRANS A/AU  
E12 18 ROSENKRANS A M/AU

=> s e2-e3 and mycobact?

L10 134 ("ROSENKRANDS I"/AU OR "ROSENKRANDS IDA"/AU) AND MYCOBACT?

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=> s l11 and tuberculosis

L12 33 L11 AND TUBERCULOSIS

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YOU HAVE REQUESTED DATA FROM 33 ANSWERS - CONTINUE? Y/ (N) :y

L12 ANSWER 1 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2006:130155 BIOSIS  
DN PREV200600112571  
TI Characterization of cationic liposomes based on dimethyldioctadecylammonium and synthetic cord factor from *M. tuberculosis* (trehalose 6,6'-dibehenate) - A novel adjuvant inducing both strong CMI and antibody responses.  
AU Davidsen, Jesper; Rosenkrands, Ida; Christensen, Dennis;  
Vangala, Anil; Kirby, Daniel; Perrie, Yvonne; Agger, Else Marie [Reprint Author]; Andersen, Peter  
CS Statens Serum Inst, Dept Infect Dis Immunol, Adjuvent Res, DK-2300 Copenhagen, Denmark  
eag@ssi.dk  
SO Biochimica et Biophysica Acta, (DEC 10 2005) Vol. 1718, No. 1-2, pp. 22-31.  
ISSN: 0005-2736.  
DT Article  
LA English  
ED Entered STN: 15 Feb 2006  
Last Updated on STN: 15 Feb 2006  
AB incorporation of the glycolipid trehalose 6,6'-dibehenate (TDB) into cationic liposomes composed of the quaternary ammonium compound dimethyldioctadecylammonium (DDA) produce an adjuvant system which induces

a powerful cell-mediated immune response and a strong antibody response, desirable for a high number of disease targets. We have used differential scanning calorimetry (DSC) to investigate the effect of TDB on the gel-fluid phase transition of DDA liposomes and to demonstrate that TDB is incorporated into DDA liposome bilayers. Transmission Electron Microscopy (TEM) and cryo-TEM confirmed that liposomes were formed when a lipid film of DDA containing small amounts of TDB was hydrated in an aqueous buffer solution at physiological pH. Furthermore, time development of particle size and zeta potential of DDA liposomes incorporating TDB during storage at 4 degrees C and 25 degrees C, indicates that TDB effectively stabilizes the DDA liposomes. Immunization of mice with the mycobacterial fusion protein Ag85B-ESAT-6 in DDA-TDB liposomes induced a strong, specific Th1 type immune response characterized by substantial production of the interferon-gamma cytokine and high levels of IgG2b isotype antibodies. The lymphocyte subset releasing the interferon-gamma was identified as CD4 T cells. (c) 2005 Published by Elsevier B.V.

L12 ANSWER 2 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2005:498396 BIOSIS  
DN PREV200510279106  
TI Cationic liposomes containing mycobacterial lipids: a new powerful Th1 adjuvant system.  
AU Rosenkrands, Ida; Agger, Else Marie [Reprint Author]; Olsen, Anja W.; Korsholm, Karen S.; Andersen, Claire Swetman; Jensen, Klaus T.; Andersen, Peter  
CS Statens Serum Inst, Dept Infect Dis Immunol, 5 Artillerivej, DK-2300 Copenhagen S, Denmark  
eag@ssi.dk  
SO Infection and Immunity, (SEP 2005) Vol. 73, No. 9, pp. 5817-5826.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 16 Nov 2005  
Last Updated on STN: 16 Nov 2005  
AB The immunostimulation provided by the mycobacterial cell wall has been exploited for many decades, e.g., in Freund's complete adjuvant. Recently, the underlying mechanism behind this adjuvant activity, including Toll receptor signaling, has begun to be unraveled, confirming the potential of mycobacterial constituents to act as adjuvants. In this study, the immunostimulatory properties of a *Mycobacterium bovis* BCG lipid extract were tested for their adjuvant activity. Administration of the lipids in dimethyl dioctadecyl ammonium bromide-based cationic liposomes induced a powerful Th1 response characterized by markedly elevated antigen-specific immunoglobulin G2a (IgG2a) isotype antibodies and substantial production of gamma interferon. The adjuvant formulation (designated mycosomes) elicited high levels of gamma interferon both in C57BL/6 as well as in Th2-prone BALB/c mice. Furthermore, the mycosomes induced immune responses to protein antigens from several sources including *Mycobacterium tuberculosis*, *Chlamydia muridarum*, and tetanus toxoid. In a *tuberculosis* challenge model, the mycosomes combined with the Ag85B-ESAT-6 fusion protein were demonstrated to have a unique ability to maintain sustained immunological memory at a level superior to live BCG.  
L12 ANSWER 3 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2005:256741 BIOSIS  
DN PREV200510047544  
TI ESAT-6 and CFP-10 in clinical versus environmental isolates of *Mycobacterium kansasii*.  
AU Arend, Sandra M. [Reprint Author]; de Haas, Petra; Leyten, Eliane; Rosenkrands, Ida; Rigouts, Leen; Andersen, Peter; Mijs, Wouter; van Dissel, Jaap T.; van Soolingen, Dick  
CS Leiden Univ, Med Ctr, Dept Infect Dis, C5P, POB 9600, NL-2300 RC Leiden, Netherlands  
s.marend@lumc.nl  
SO Journal of Infectious Diseases, (APR 15 2005) Vol. 191, No. 8, pp. 1301-1310.  
CODEN: JIDIAQ. ISSN: 0022-1899.  
DT Article

LA English  
ED Entered STN: 14 Jul 2005  
Last Updated on STN: 14 Jul 2005  
AB **Mycobacterium kansasii** consists of 5 genetically distinct groups, of which 2 are associated with human disease. Determinants of the differences in virulence are unknown. Potential genes of interest are esat-6 and cfp-10, which are associated with virulence of **Mycobacterium tuberculosis** and **Mycobacterium bovis** but are lacking in bacille Calmette-Guerin and in most environmental mycobacteria (*M. kansasii* is an exception). We investigated esat-6 and cfp-10 genes in 22 clinical and 14 environmental isolates of *M. kansasii*. Both were present in all isolates; each genetic group had its own characteristic Southern-blot pattern corresponding to a highly conserved fingerprint pattern. Nucleotide sequences of the genes differed 12.6% and 10.1%, respectively, from the *M. tuberculosis* homologues, but the deduced amino acid sequences were <5% different. In vitro, clinical and environmental genotypes of *M. kansasii* expressed CFP-10 and ESAT-6. Thus, virulence of *M. kansasii* is not directly related to esat-6 and cfp-10 genes or gene expression.

L12 ANSWER 4 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2005:240405 BIOSIS  
DN PREV200510029170  
TI Differential effects of prior exposure to environmental mycobacteria on vaccination with **Mycobacterium bovis** BCG or a recombinant BCG strain expressing RD1 antigens.  
AU Demangel, Caroline [Reprint Author]; Garnier, Thierry; Rosenkrands, Ida; Cole, Stewart T.  
CS Inst Pasteur, Unite Genet Mol Bacterienne, 28 Rue Dr Roux, F-75724 Paris, France  
demangel@pasteur.fr  
SO Infection and Immunity, (APR 2005) Vol. 73, No. 4, pp. 2190-2196.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 29 Jun 2005  
Last Updated on STN: 29 Jun 2005  
AB In silico analysis reveals that most protective antigens expressed by the antituberculous vaccine **Mycobacterium bovis** BCG (BCG) are conserved in *M. avium*, supporting the hypothesis that exposure to environmental mycobacteria generates cross-reactive immune responses blocking BCG activity. We investigated the impact of sensitization with *M. avium*, *M. scrofulaceum*, or *M. vaccae* on the protective efficacy of a recombinant BCG strain expressing RD1 antigens (BCG::RD1), using a mouse model of experimental tuberculosis (TB). No evidence that the RD1-encoded antigens ESAT-6, CFP-10, and PPE68 were expressed by these environmental strains could be demonstrated by Western blot analysis. Mice sensitized with each of these strains did not prime cellular immune responses cross-reacting with the immunodominant ESAT-6. Importantly, clearance of BCG::RD1 from the lungs and spleens of mice exposed to each of the environmental strains before vaccination was minimal compared to that of BCG. In mice sensitized with *M. avium*, increased persistence of BCG::RD1 correlated with stronger antimycobacterial gamma interferon responses and enhanced protection against aerosol infection with *M. tuberculosis*, compared to BCG. In contrast, animals exposed to *M. scrofulaceum* or *M. vaccae* prior to vaccination with BCG or BCG::RD1 were better protected against TB than were the unsensitized controls. Our results suggest that the inhibitory effect of environmental mycobacteria on the protective efficacy of BCG depends critically on the extent of cross-recognition of antigens shared with the vaccine. In hosts sensitized with *M. avium*, potent immunogenicity of ESAT-6 and increased persistence of BCG::RD1 may allow this recombinant vaccine to overcome preexisting antimycobacterial responses.

L12 ANSWER 5 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2005:55794 BIOSIS  
DN PREV200500051999  
TI ESAT-6 proteins: protective antigens and virulence factors?.

AU Brodin, Priscille; Rosenkrands, Ida; Andersen, Peter; Cole, Stewart T. [Reprint Author]; Brosch, Roland  
CS Unite Genet Mol Bacterienne, Inst Pasteur, 28 Rue Dr Roux, F-75724, Paris, France  
stcole@pasteur.fr  
SO Trends in Microbiology, (November 2004) Vol. 12, No. 11, pp. 500-508.  
print.  
ISSN: 0966-842X (ISSN print).  
DT Article  
LA General Review; (Literature Review)  
ED English  
Entered STN: 3 Feb 2005  
Last Updated on STN: 3 Feb 2005  
AB The 6 kDa early secreted antigenic target from *Mycobacterium tuberculosis*, ESAT-6, is the prototype of a novel family of small proteins of unknown function produced by Actinobacteria. Export of ESAT-6, a potent T-cell antigen, and related proteins requires a dedicated secretory apparatus that is encoded by a cluster of genes, several of which also code for proteins that are recognized strongly by T cells. ESAT-6 systems can thus be considered as immunogenicity islands and there is growing evidence that the corresponding genes are subject to selective pressure imposed by the immune system of the host. Recently, there has been major progress in understanding the biogenesis, secretion and antigenicity of ESAT-6 proteins and, at least in the case of ESAT-6 system 1, in unravelling their role in pathogenicity. Here, we discuss these findings and their implications for the development of new therapeutic and prophylactic interventions against *tuberculosis*.

L12 ANSWER 6 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2005:26452 BIOSIS  
DN PREV200500027841  
TI CFP10 discriminates between nonacetylated and acetylated ESAT-6 of *Mycobacterium tuberculosis* by differential interaction.  
AU Okkels, Limei Meng; Mueller, Eva-Christina; Schmid, Monika; Rosenkrands, Ida; Kaufmann, Stefan H. E.; Andersen, Peter; Jungblut, Peter R. [Reprint Author]  
CS Core Facil Prot Anal, Max Planck Inst Infect Biol, Schumannstr 21-22, D-10117, Berlin, Germany  
jungblut@mpiib-berlin.mpg.de  
SO Proteomics, (October 2004) Vol. 4, No. 10, pp. 2954-2960. print.  
ISSN: 1615-9853 (ISSN print).  
DT Article  
LA English  
ED Entered STN: 5 Jan 2005  
Last Updated on STN: 5 Jan 2005  
AB ESAT-6 (the 6 kDa early secreted antigenic target) protein species in short-term culture filtrate of *Mycobacterium tuberculosis* were separated in a 4-5 narrow range p/ gradient two-dimensional gel electrophoresis (2-DE). Eight ESAT-6 protein species were analyzed in detail by peptide mass fingerprinting matrix-assisted laser desorption/ionization-mass spectrometry as well as by electrospray ionization-tandem mass spectrometry. An N-terminal Thr acetylation was identified in four species and a C-terminal truncation was identified in two species. In 2-DE blot overlay assays, the recombinant 10 kDa culture filtrate protein (CFP10) discriminated N-terminal acetylated and nonacetylated ESAT-6 by differential interaction, whereas removal of the C-terminal 11 residues of ESAT-6 had no effects thereon. This example shows that the access to the protein species level can be a prerequisite to understand regulation of protein-protein interaction.

L12 ANSWER 7 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2004:33002 BIOSIS  
DN PREV200400035432  
TI PPE protein (Rv3873) from DNA segment RD1 of *Mycobacterium tuberculosis*: Strong recognition of both specific T-cell epitopes and epitopes conserved within the PPE family.  
AU Okkels, Limei Meng [Reprint Author]; Brock, Inger; Follmann, Frank; Agger, Else Marie; Arend, Sandra M.; Ottenhoff, Tom H. M.; Oftung, Fredrik; Rosenkrands, Ida; Andersen, Peter

CS Department of Infectious Disease Immunology, Statens Serum Institut,  
Artillerivej 5, DK-2300, Copenhagen, Denmark  
lmo@ssi.dk

SO Infection and Immunity, (November 2003) Vol. 71, No. 11, pp. 6116-6123.  
print.  
ISSN: 0019-9567 (ISSN print).

DT Article  
LA English  
ED Entered STN: 7 Jan 2004  
Last Updated on STN: 7 Jan 2004

AB Proteins encoded by DNA segment RD1 of **Mycobacterium tuberculosis** have recently been demonstrated to play important roles in bacterial virulence, vaccine development, and diagnostic reagent design. Previously, we characterized two immunodominant T-cell antigens, the early secreted antigen target (ESAT-6), and the 10-kDa culture filtrate protein (CFP10), which are encoded by the esx-1hp operon in this region. In the present study we characterized a third putative open reading frame in this region, rv3873, which encodes a PPE protein. We found that the rv3873 gene is expressed in *M. tuberculosis* H37Rv and that the native protein, Rv3873, is predominantly associated with the mycobacterial cell or wall. When tested as a His-tagged recombinant protein, Rv3873 stimulated high levels of gamma interferon secretion in peripheral blood mononuclear cells isolated from **tuberculosis** (TB) patients, as well as from healthy tuberculin purified protein derivative-positive donors. In contrast to other RD1-encoded antigens, Rv3873 was also found to be recognized by a significant proportion of **Mycobacterium bovis** BCG-vaccinated donors. Epitope mapping performed with overlapping peptides revealed a broad pattern of T-cell recognition comprising both TB-specific epitopes and epitopes also recognized by BCG-vaccinated donors. The immunodominant epitope (residues 118 to 135) for both TB patients and BCG-vaccinated individuals was found to be highly conserved among a large number of PPE family members.

L12 ANSWER 8 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2004:5335 BIOSIS  
DN PREV200400007544

TI Nucleic acids fragments and polypeptide fragments derived from *M. tuberculosis*.

AU Andersen, Peter [Inventor, Reprint Author]; Nielsen, Rikke [Inventor]; Oettinger, Thomas [Inventor]; Rasmussen, Peter Birk [Inventor]; Rosenkrands, Ida [Inventor]; Weldingh, Karin [Inventor]; Florio, Walter [Inventor]

CS Bronshoj, Denmark  
ASSIGNEE: Statens Serum Institut, Copenhagen, Denmark  
PI US 6641814 20031104

SO Official Gazette of the United States Patent and Trademark Office Patents, (Nov 4 2003) Vol. 1276, No. 1. <http://www.uspto.gov/web/menu/patdata.html>.  
e-file.  
ISSN: 0098-1133 (ISSN print).

DT Patent  
LA English  
ED Entered STN: 17 Dec 2003  
Last Updated on STN: 17 Dec 2003

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L12 ANSWER 9 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2003:34905 BIOSIS  
DN PREV200300034905

TI Specific acquired resistance in mice immunized with killed mycobacteria.  
AU Agger, E. M.; Weldingh, K.; Olsen, A. W.; Rosenkrands, I.; Andersen, P. [Reprint Author]  
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen, Denmark pa@ssi.dk  
SO Scandinavian Journal of Immunology, (November 2002) Vol. 56, No. 5, pp. 443-447. print.  
ISSN: 0300-9475 (ISSN print).  
DT Article  
LA English  
ED Entered STN: 8 Jan 2003  
Last Updated on STN: 8 Jan 2003  
AB Past attempts to raise resistance against **Mycobacterium tuberculosis** using various preparations of killed mycobacteria have questioned the specificity of the generated immune response. In the present study, we have focused on the protective efficacy of experimental vaccines based on killed mycobacteria. We demonstrate that killed mycobacteria can confer high levels of protection, which can be adoptively transferred to recipient T-cell-deficient mice. Moreover, protective antigens can be found in the cell wall, membrane and cytosol of the mycobacterial cell, and hence emphasize the importance of searching for protective antigens in various compartments of the mycobacterial cell.

L12 ANSWER 10 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2002:364515 BIOSIS  
DN PREV200200364515  
TI Hypoxic response of **Mycobacterium tuberculosis** studied by metabolic labeling and proteome analysis of cellular and extracellular proteins.  
AU Rosenkrands, Ida [Reprint author]; Slayden, Richard A.; Crawford, Janne; Aagaard, Claus; Barry, Clifton E., III; Andersen, Peter  
CS Department of TB Immunology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen S, Denmark idr@ssi.dk  
SO Journal of Bacteriology, (July, 2002) Vol. 184, No. 13, pp. 3485-3491. print.  
CODEN: JOBAAY. ISSN: 0021-9193.  
DT Article  
LA English  
ED Entered STN: 3 Jul 2002  
Last Updated on STN: 3 Jul 2002  
AB The events involved in the establishment of a latent infection with **Mycobacterium tuberculosis** are not fully understood, but hypoxic conditions are generally believed to be the environment encountered by the pathogen in the central part of the granuloma. The present study was undertaken to provide insight into **M. tuberculosis** protein expression in *in vitro* latency models where oxygen is depleted. The response of **M. tuberculosis** to low-oxygen conditions was investigated in both cellular and extracellular proteins by metabolic labeling, two-dimensional electrophoresis, and protein signature peptide analysis by liquid chromatography-mass spectrometry. By peptide mass fingerprinting and immunodetection, five proteins more abundant under low-oxygen conditions were identified from several lysates of **M. tuberculosis**: Rv0569, Rv2031c (HspX), Rv2623, Rv2626c, and Rv3841 (BfrB). In **M. tuberculosis** culture filtrates, two additional proteins, Rv0363c (Fba) and Rv2780 (Ald), were found in increased amounts under oxygen limitation. These results extend our understanding of the hypoxic response in **M. tuberculosis** and potentially provide important insights into the physiology of the latent bacilli.

L12 ANSWER 11 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2001:37127 BIOSIS  
DN PREV200100037127

TI Towards the proteome of **Mycobacterium tuberculosis**.  
AU Rosenkrands, Ida [Reprint author]; King, Angus; Weldingh, Karin;  
Moniatte, Marc; Moertz, Ej vind; Andersen, Peter  
CS Department of TB Immunology, Statens Serum Institut, 5 Artillerivej,  
DK-2300, Copenhagen S, Denmark  
idr@ssi.dk  
SO Electrophoresis, (November, 2000) Vol. 21, No. 17, pp. 3740-3756. print.  
CODEN: ELCTDN. ISSN: 0173-0835.  
DT Article  
LA English  
ED Entered STN: 17 Jan 2001  
Last Updated on STN: 12 Feb 2002  
AB Human tuberculosis is caused by the intracellular pathogen **Mycobacterium tuberculosis**. Sequencing of the genome of *M. tuberculosis* strain H37Rv has predicted 3924 open reading frames, and enabled identification of proteins from this bacterium by peptide mass fingerprinting. Extracellular proteins from the culture medium and proteins in cellular extracts were examined by two-dimensional gel electrophoresis using immobilized pH gradient technology. By mass spectrometry and immunodetection, 49 culture filtrate proteins and 118 lysate proteins were identified, 83 of which were novel. To date, 288 proteins have been identified in *M. tuberculosis* proteome studies, and a list is presented which includes all identified proteins (available at <http://www.ssi.dk/publichealth/tbimmun>). The information obtained from the *M. tuberculosis* proteome so far is discussed in relation to the information obtained from the complete genome sequence.

L12 ANSWER 12 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 2000:271567 BIOSIS

DN PREV200000271567

TI Mapping and identification of **Mycobacterium tuberculosis** proteins by two-dimensional gel electrophoresis, microsequencing and immunodetection.

AU Rosenkrands, Ida; Weldingh, Karin; Jacobsen, Susanne; Hansen, Christina Vegerby; Florio, Walter; Gianetri, Isabella; Andersen, Peter [Reprint author]

CS Department of TB Immunology, Statens Serum Institute, 5 Artillerivej, DK-2300, Copenhagen S, Denmark

SO Electrophoresis, (March, 2000) Vol. 21, No. 5, pp. 935-948. print.  
CODEN: ELCTDN. ISSN: 0173-0835.

DT Article

LA English

ED Entered STN: 30 Jun 2000

Last Updated on STN: 5 Jan 2002

AB **Mycobacterium tuberculosis** is the infectious agent giving rise to human **tuberculosis**. The entire genome of *M. tuberculosis*, comprising approximately 4000 open reading frames, has been sequenced. The huge amount of information released from this project has facilitated proteome analysis of *M. tuberculosis*. Two-dimensional polyacrylamide gel electrophoresis (2-D PAGE) was applied to fractions derived from *M. tuberculosis* culture filtrate, cell wall, and cytosol, resulting in the resolution of 376, 413, and 395 spots, respectively, in silver-stained gels. By microsequencing and immunodetection, 38 culture filtrate proteins were identified and mapped, of which 12 were identified for the first time. In the same manner, 23 cell wall proteins and 19 cytosol proteins were identified and mapped, with 9 and 10, respectively, being novel proteins. One of the novel proteins was not predicted in the genome project, and for four of the identified proteins alternative start codons were suggested. Fourteen of the culture filtrate proteins were proposed to possess signal sequences. Seven of these proteins were microsequenced and the N-terminal sequences obtained confirmed the prediction. The data presented here are an important complement to the genetic information, and the established 2-D PAGE maps (also available at: [www.ssi.dk/publichealth/tbimmun](http://www.ssi.dk/publichealth/tbimmun)) provide a basis for comparative studies of protein expression.

L12 ANSWER 13 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 2000:110101 BIOSIS  
DN PREV200000110101  
TI ESAT-6 subunit vaccination against **Mycobacterium tuberculosis**.  
AU Brandt, Lise; Elhay, Martin; Rosenkrands, Ida; Lindblad, Erik B.; Andersen, Peter [Reprint author]  
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, 2300, Copenhagen S., Denmark  
SO Infection and Immunity, (Feb., 2000) Vol. 68, No. 2, pp. 791-795. print.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 22 Mar 2000  
Last Updated on STN: 3 Jan 2002  
AB The ESAT-6 antigen from **Mycobacterium tuberculosis** is a dominant target for cell-mediated immunity in the early phase of tuberculosis (TB) in TB patients as well as in various animal models. The purpose of our study was to evaluate the potential of ESAT-6 in an experimental TB vaccine. We started out using dimethyl dioctadecylammonium bromide (DDA), an adjuvant which has been demonstrated to be efficient for the induction of cellular immune responses and has been used successfully before as a delivery system for TB vaccines. Here we demonstrate that, whereas immune responses to both short-term-culture filtrate and AG85B are efficiently induced with DDA, this adjuvant was inefficient for the induction of immune responses to ESAT-6. Therefore, we investigated the modulatory effect of monophosphoryl lipid A (MPL), an immunomodulator which in different combinations has demonstrated strong adjuvant activity for both cellular and humoral immune responses. We show in the present study that vaccination with ESAT-6 delivered in a combination of MPL and DDA elicited a strong ESAT-6-specific T-cell response and protective immunity comparable to that achieved with **Mycobacterium bovis** BCG.

L12 ANSWER 14 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 2000:104643 BIOSIS  
DN PREV200000104643  
TI Comparative evaluation of low-molecular-mass proteins from **Mycobacterium tuberculosis** identifies members of the ESAT-6 family as immunodominant T-cell antigens.  
AU Skjot, Rikke Louise Vinther; Oettinger, Thomas; Rosenkrands, Ida ; Ravn, Pernille; Brock, Inger; Jacobsen, Susanne; Andersen, Peter [Reprint author]  
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark  
SO Infection and Immunity, (Jan., 2000) Vol. 68, No. 1, pp. 214-220. print.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 22 Mar 2000  
Last Updated on STN: 3 Jan 2002  
AB Culture filtrate from **Mycobacterium tuberculosis** contains protective antigens of relevance for the generation of a new antituberculosis vaccine. We have identified two previously uncharacterized **M. tuberculosis** proteins (TB7.3 and TB10.4) from the highly active low-mass fraction of culture filtrate. The molecules were characterized, mapped in a two-dimensional electrophoresis reference map of short-term culture filtrate, and compared with another recently identified low-mass protein, CFP10 (F. X. Berthet, P. B. Rasmussen, I. Rosenkrands, P. Andersen, and B. Gicquel. Microbiology 144:3195-3203, 1998), and the well-described ESAT-6 antigen. Genetic analyses demonstrated that TB10.4 as well as CFP10 belongs to the ESAT-6 family of low-mass proteins, whereas TB7.3 is a low-molecular-mass protein outside this family. The proteins were expressed in *Escherichia coli*, and their immunogenicity was tested in cultures of peripheral blood mononuclear cells from human **tuberculosis** (TB) patients, **Mycobacterium bovis** BCG-vaccinated donors, and nonvaccinated donors. The two ESAT-6 family members, TB10.4 and CFP10, were very strongly recognized and induced gamma interferon release at the same level

(CFP10) as or at an even higher level (TB10.4) than ESAT-6. The non-ESAT-6 family member, TB7.3, for comparison, was recognized at a much lower level. CFP10 was found to distinguish TB patients from BCG-vaccinated donors and is, together with ESAT-6, an interesting candidate for the diagnosis of TB. The striking immunodominance of antigens within the ESAT-6 family is discussed, and hypotheses are presented to explain this targeting of the immune response during TB infection.

L12 ANSWER 15 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 2000:34114 BIOSIS

DN PREV200000034114

TI Differential T-cell recognition of native and recombinant *Mycobacterium tuberculosis* GroES.

AU Rosenkrands, Ida; Weldingh, Karin; Ravn, Pernille; Brandt, Lise; Hojrup, Peter; Rasmussen, Peter Birk; Coates, Anthony R.; Singh, Mahavir; Mascagni, Paolo; Andersen, Peter [Reprint author]

CS Department of TB Immunology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen S, Denmark

SO Infection and Immunity, (Nov., 1999) Vol. 67, No. 11, pp. 5552-5558. print.

CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English

ED Entered STN: 19 Jan 2000

Last Updated on STN: 31 Dec 2001

AB *Mycobacterium tuberculosis* GroES was purified from culture filtrate, and its identity was confirmed by immunoblot analysis and N-terminal sequencing. Comparing the immunological recognition of native and recombinant GroES, we found that whereas native GroES elicited a strong proliferative response and release of gamma interferon-gamma by peripheral blood mononuclear cells from healthy tuberculin reactors, the recombinant protein failed to do so. The same difference in immunological recognition was observed in a mouse model of TB infection. Both the native and recombinant preparations were recognized by mice immunized with the recombinant protein. Biochemical characterization including sodium dodecyl sulfate-polyacrylamide gel electrophoresis, two-dimensional electrophoresis, and mass spectrometry analysis of both proteins demonstrated no differences between the native and recombinant forms of GroES except for the eight additional N-terminal amino acids derived from the fusion partner inrecombinant GroES. The recombinant fusion protein, still tagged with the maltose binding protein, was recognized by T cells isolated from TB-infected mice if mixed with culture filtrate before affinity purification on an amylose column. The maltose binding protein treated in the same manner as a control preparation was not recognized. Based on the data presented, we suggest that the association of biologically active molecules from culture filtrate with the chaperone GroES may be responsible for the observed T-cell recognition of the native preparation.

L12 ANSWER 16 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 1999:197118 BIOSIS

DN PREV199900197118

TI Human T cell responses to the ESAT-6 antigen from *Mycobacterium tuberculosis*.

AU Ravn, Pernille; Demissie, Abebech; Eguale, Tewodros; Wondwosson, Hailu; Lein, David; Amoudy, Hanady A.; Mustafa, Abu S.; Jensen, Axel Kok; Holm, Arne; Rosenkrands, Ida; Oftung, Fredrik; Olobo, Joseph; von Reyn, Fordham; Andersen, Peter [Reprint author]

CS Dept. of TB Immunology, Statens Serum Institut, Artillerivej 5, 2300 S, Denmark

SO Journal of Infectious Diseases, (March, 1999) Vol. 179, No. 3, pp. 637-645. print.

CODEN: JIDIAQ. ISSN: 0022-1899.

DT Article

LA English

ED Entered STN: 25 May 1999

AB Last Updated on STN: 25 May 1999

Human T cell responses to ESAT-6 and eight synthetic overlapping peptides were investigated in *tuberculosis* (TB) patients and control subjects from regions of high and low endemicity for TB. ESAT-6 was recognized by 65% of all tuberculin purified protein derivative-responsive TB patients, whereas only 2 of 29 bacille Calmette-Guerin-vaccinated Danish healthy donors recognized this molecule. In Ethiopia, a high frequency (58%) of healthy contacts of TB patients recognized ESAT-6. All of the peptides were recognized by some donors, indicating that the molecule holds multiple epitopes. Danish and Ethiopian patients differed in the fine specificity of their peptide responses. Recognition of the C-terminal region (aa 72-95) was predominant in Danish patients, whereas recognition of aa 42-75 was predominant in Ethiopia. The relationship of these differences to the distribution of HLA types in the two populations is discussed. This study demonstrates that ESAT-6 is frequently recognized during early infection and holds potential as a component of a future TB-specific diagnostic reagent.

L12 ANSWER 17 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 1999:28278 BIOSIS

DN PREV199900028278

TI A *Mycobacterium tuberculosis* operon encoding ESAT-6 and a novel low-molecular-mass culture filtrate protein (CFP-10).

AU Berthet, Francois-Xavier [Reprint author]; Rasmussen, Peter Birk; Rosenkrands, Ida; Andersen, Peter; Gicquel, Brigitte

CS Unite Geneitque Mycobacteriene, Inst. Pasteur, 25 rue Dr Roux, 75724 Paris Cedex 15, France

SO Microbiology (Reading), (Nov., 1998) Vol. 144, No. 11, pp. 3195-3203. print.

ISSN: 1350-0872.

DT Article

LA English

OS Genbank-AF004671

ED Entered STN: 3 Feb 1999

Last Updated on STN: 3 Feb 1999

AB The early secreted antigenic target 6 kDa protein (ESAT-6) is a potent T-cell protein antigen synthesized by *Mycobacterium tuberculosis*. Its corresponding gene (esat-6) is located in RD1, a 10 kb DNA region deleted in the attenuated *tuberculosis* vaccine strain *Mycobacterium bovis* BCG. The promoter region of *M. tuberculosis* esat-6 was cloned and characterized. A new gene, designated lhp and cotranscribed with esat-6, was identified. Moreover, computer searches in the *M. tuberculosis* genome identified 13 genes related to the lhp/esat-6 operon, defining a novel gene family. The transcription initiation sites of the lhp/esat-6 operon were mapped using *M. tuberculosis* RNA. The corresponding promoter signals were not recognized in *Mycobacterium smegmatis*, in which transcription of lhp/esat-6 is initiated at different locations. The *M. tuberculosis* lhp gene product was identified as CFP-10, a low-molecular-mass protein found in the short-term culture filtrate. These results show that the genes encoding CFP-10 and ESAT-6 are transcribed together in *M. tuberculosis* and that both code for small exported proteins.

L12 ANSWER 18 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 1998:393332 BIOSIS

DN PREV199800393332

TI Two-dimensional electrophoresis for analysis of *Mycobacterium tuberculosis* culture filtrate and purification and characterization of six novel proteins.

AU Weldingh, Karin; Rosenkrands, Ida; Jacobsen, Susanne; Rasmussen, Peter Birk; Elhay, Martin J.; Andersen, Peter [Reprint author]

CS Dep. TB Immunol., Statens Serum Inst., Artillerivej 5, DK-2300 Copenhagen, Denmark

SO Infection and Immunity, (Aug., 1998) Vol. 66, No. 8, pp. 3492-3500. print. CODEN: INFIBR. ISSN: 0019-9567.

DT Article

LA English  
ED Entered STN: 10 Sep 1998  
Last Updated on STN: 10 Sep 1998  
AB Culture filtrate from **Mycobacterium tuberculosis**  
contains molecules which promote high levels of protective immunity in animal models of subunit vaccination against **tuberculosis**. We have used two-dimensional electrophoresis for analysis and purification of six novel *M. tuberculosis* culture filtrate proteins (CFPs): CFP17, CFP20, CFP21, CFP22, CFP25, and CFP28. The proteins were tested for recognition by *M. tuberculosis*-reactive memory cells from different strains of inbred mice and for their capacity to induce a skin test response in *M. tuberculosis*-infected guinea pigs. CFP17, CFP20, CFP21 and CFP25 induced both a high gamma interferon release and a strong delayed-type hypersensitivity response, and CFP21 was broadly recognized by different strains of inbred mice. N-terminal sequences were obtained for the six proteins, and the corresponding genes were identified in the Sanger *M. tuberculosis* genome database. In parallel we established a two-dimensional electrophoresis reference map of short-term culture filtrate components and mapped novel proteins as well as already-known CFP.  
  
L12 ANSWER 19 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
  
AN 1998:304925 BIOSIS  
DN PREV199800304925  
TI Identification and characterization of a 29-kilodalton protein from **Mycobacterium tuberculosis** culture filtrate recognized by mouse memory effector cells.  
AU Rosenkrands, Ida; Rasmussen, Peter Birk; Carnio, Markus;  
Jacobsen, Susanne; Theisen, Michael; Andersen, Peter [Reprint author]  
CS Dep. TB Immunol., Statens Serum Inst., 5 Artillerivej, DK-2300 Copenhagen S, Denmark  
SO Infection and Immunity, (June, 1998) Vol. 66, No. 6, pp. 2728-2735. print.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
OS Genbank-Y12820; EMBL-Y12820; DDBJ-Y12820  
ED Entered STN: 15 Jul 1998  
Last Updated on STN: 15 Jul 1998  
AB Culture filtrate proteins from **Mycobacterium tuberculosis** induce protective immunity in various animal models of **tuberculosis**. Two molecular mass regions (6 to 10 kDa and 24 to 36 kDa) of short-term culture filtrate are preferentially recognized by Th1 cells in animal models as well as by patients with minimal disease. In the present study, the 24- to 36-kDa region has been studied, and the T-cell reactivity has been mapped in detail. Monoclonal antibodies were generated, and one monoclonal antibody, HYB 71-2, with reactivity against a 29-kDa antigen located in the highly reactive region below the antigen 85 complex was selected. The 29-kDa antigen (CFP29) was purified from *M. tuberculosis* short-term culture filtrate by thiophilic adsorption chromatography, anion-exchange chromatography, and gel filtration. In its native form, CFP29 forms a polymer with a high molecular mass. CFP29 was mapped in two-dimensional electrophoresis gels as three distinct spots just below the antigen 85 complex component MPT59. CFP29 is present in both culture filtrate and the membrane fraction from *M. tuberculosis*, suggesting that this antigen is released from the envelope to culture filtrate during growth. Determination of the N-terminal amino acid sequence allowed cloning and sequencing of the cfp29 gene. The nucleotide sequence showed 62% identity to the bacteriocin Linocin from *Brevibacterium linens*. Purified recombinant histidine-tagged CFP29 and native CFP29 had similar T-cell stimulatory properties, and they both elicited the release of high levels of gamma interferon from mouse memory effector cells isolated during the recall of protective immunity to **tuberculosis**. Interspecies analysis by immunoblotting and PCR demonstrated that CFP29 is widely distributed in **mycobacterial** species.  
  
L12 ANSWER 20 OF 33 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

AN 1996:76919 BIOSIS  
DN PREV199698649054  
TI Evidence for occurrence of the ESAT-6 protein in **Mycobacterium tuberculosis** and virulent **Mycobacterium bovis** and for its absence in **Mycobacterium bovis** BCG.  
AU Harboe, Morten [Reprint author]; Oettinger, Thomas; Wiker, Harald Gotten; Rosenkrands, Ida; Andersen, Peter  
CS Inst. Immunol. Rheumatol., Univ. Oslo, N-0172 Oslo, Norway  
SO Infection and Immunity, (1996) Vol. 64, No. 1, pp. 16-22.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 27 Feb 1996  
Last Updated on STN: 27 Feb 1996  
AB ESAT-6 is a secreted protein present in the short-term culture filtrate of **Mycobacterium tuberculosis** after growth on a synthetic Sauton medium. ESAT-6 has recently been demonstrated to induce strong T-cell responses in a mouse model of memory immunity after infection with **M. tuberculosis**. In Western blotting (immunoblotting), the monoclonal antibody HYB76-8, reacting with ESAT-6, gave a 6-kDa band in culture filtrates from **M. tuberculosis** and virulent **Mycobacterium bovis**. A distinct band in the 24-kDa region was observed in filtrates from four of eight substrains of **M. bovis** BCG that produced high levels of MPB64, while no band occurred in the 6-kDa region with any of these BCG substrains. Southern blotting and PCR experiments with genomic mycobacterial DNA showed the presence of the esat-6 gene in reference strains and clinical isolates of **V. tuberculosis** as well as in virulent **M. bovis**. The esat-6 gene could not be demonstrated in any of the eight substrains of **M. bovis** BCG tested by these techniques. Two gene deletions that distinguish **M. bovis** BCG from virulently **M. bovis** have thus now been demonstrated. Deletion of mpb64 affects four of the eight substrains tested; deletion of esat-6 affects all of them. The reaction of HYB76-8 at 26 kDa with four of the BCG substrains was demonstrated to result from cross-reactivity with MPB64. HYB76-8 was also shown to cross-react with the A, B, and C components of the antigen 85 complex and MPT51.

L12 ANSWER 21 OF 33 CABA COPYRIGHT 2006 CABI on STN  
AN 2003:125917 CABA  
DN 20033096065  
TI Specific delayed-type hypersensitivity responses to ESAT-6 identify **tuberculosis**-infected cattle  
AU Pollock, J. M.; McNair, J.; Bassett, H.; Cassidy, J. P.; Costello, E.; Aggerbeck, H.; Rosenkrands, I.; Andersen, P.  
CS Veterinary Sciences Division, Department of Agriculture and Rural Development, Stoney Rd., Stormont, Belfast BT4 3SD, UK.  
john.pollock@dardni.gov.uk  
SO Journal of Clinical Microbiology, (2003) Vol. 41, No. 5, pp. 1856-1860. 34 ref.  
Publisher: American Society for Microbiology (ASM). Washington  
ISSN: 0095-1137  
DOI: 10.1128/JCM.41.5.1856-1860.2003  
CY United States  
DT Journal  
LA English  
ED Entered STN: 12 Aug 2003  
Last Updated on STN: 12 Aug 2003  
AB Human and bovine **tuberculosis** have long been detected by skin testing with purified protein derivative (PPD), a complex mix of partly denatured mycobacterial antigens with suboptimal specificity. In the present study, skin tests based on ESAT-6, a recombinantly produced antigen highly specific for **tuberculosis** infection, were investigated. Although ESAT-6 was strongly recognized in vitro and induced high levels of gamma interferon, initial investigations demonstrated that higher doses of ESAT-6 than of PPD were needed to induce substantial delayed-type hypersensitivity reactions. Also, the kinetics of the skin test response differed for the two reagents; PPD showed maximal response at 72 h, but the response to ESAT-6 often peaked later at 96 h. Tests based on an optimized strategy (400 [micro]g of ESAT-6 measured between 72

and 96 h), in cattle infected with *Mycobacterium bovis* (n=22) and animals sensitized by exposure to environmental mycobacteria showed ESAT-6 to have a promising diagnostic potential (sensitivity, 82%; specificity, 100%; optimal cutoff, 3 mm), compared with PPD (sensitivity, 86%; specificity, 90%; optimal cutoff, 4 mm). Larger investigations are required to refine cutoff points for any new diagnostic test, but the present results indicate great potential for skin tests based on specific antigens for accurate in vivo diagnosis of tuberculosis.

L12 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2005:119461 CAPLUS  
DN 142:334537  
TI Assessing the serodiagnostic potential of 35 *Mycobacterium tuberculosis* proteins and identification of four novel serological antigens  
AU Weldingh, Karin; Rosenkrands, Ida; Okkels, Limei Meng; Doherty, T. Mark; Andersen, Peter  
CS Department of Infectious Disease Immunology, Statens Serum Institut, Copenhagen, Den.  
SO Journal of Clinical Microbiology (2005), 43(1), 57-65  
CODEN: JCMIDW; ISSN: 0095-1137  
PB American Society for Microbiology  
DT Journal  
LA English  
AB Improved diagnostic reagents are needed for the detection of *Mycobacterium tuberculosis* infections, and the development of a serodiagnostic test would complement presently available diagnostic methods. The aim of the present study was to identify novel serol. targets for use for the future serodiagnosis of tuberculosis (TB). The authors cloned and expressed 35 M. tuberculosis proteins as recombinant proteins in Escherichia coli and analyzed their serodiagnostic potentials. By a two-step selection process, four superior seroantigens, TB9.7, TB15.3, TB16.3, and TB51, were identified, none of which has been described before. The four novel antigens were tested with panels of sera from smear-pos. and smear-neg. TB patients from areas both where TB is endemic and where TB is not endemic, with recognition frequencies ranging from 31 to 93% and with a specificity of at least 97%. The single most potent antigen was TB16.3, which had a sensitivity of 48 to 55% with samples from Danish resident TB patients and a sensitivity of 88 to 98% with samples from African TB patients. Importantly, the TB16.3 and the TB9.7 antigens were recognized by more than 85% of the samples from TB patients coinfected with human immunodeficiency virus, a patient group for which it is in general difficult to detect M. tuberculosis-specific antibodies.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2005:55095 CAPLUS  
DN 142:133056  
TI Vaccines comprising cationic surfactant and lipid extract of *Mycobacterium BCG* as adjuvant for treating cancer, allergy and autoimmune disease  
IN Agger, Else Marie; Andersen, Peter; Olsen, Anja; Rosenkrands, Ida  
PA Statens Serum Institut, Den.  
SO PCT Int. Appl., 52 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
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PI	WO 2005004911	A2	20050120	WO 2004-DK488	20040707	
	WO 2005004911	A3	20050217			
	WO 2005004911	B1	20050317			
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,  
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
 SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE,  
 SN, TD, TG

AU 2004255393	A1	20050120	AU 2004-255393	20040707
CA 2531825	AA	20050120	CA 2004-2531825	20040707
PRAI DK 2003-1046	A	20030709		
DK 2003-1403	A	20030927		
WO 2004-DK488	W	20040707		

**AB** The present invention provides a vaccine adjuvant consisting of a combination of a surfactant i.e. dimethyldodecylammonium-bromide/chloride (DDA) and a lipid extract from *Mycobacterium bovis* BCG. The total lipid extract contains both apolar lipids, polar lipids, and lipids of intermediate polarity of which the apolar lipids were found to induce the most powerful immune responses. The total lipids may be extracted with chloroform/methanol and re-dissolved in water before the addition of surfactant. This preparation may be used to induce prominent cell-mediated immune responses in a mammal in order to combat pathogens, or as a treatment for cancer.

L12 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:1050159 CAPLUS  
 DN 142:312800  
 TI The proteome of *Mycobacterium tuberculosis*  
 AU Belisle, John T.; Braunstein, Miriam; Rosenkrands, Ida;  
 Andersen, Peter  
 CS Mycobacteria Research Laboratories, Department of Microbiology,  
 Immunology, and Pathology, Colorado State University, Fort Collins, CO,  
 80523, USA  
 SO Tuberculosis and the Tubercl Bacillus (2005), 235-260. Editor(s): Cole,  
 Stewart T. Publisher: American Society for Microbiology, Washington, D. C.  
 CODEN: 69GFRV; ISBN: 1-55581-295-3  
 DT Conference; General Review  
 LA English  
 AB A review on current understanding of the *Mycobacterium tuberculosis* proteome, including unique aspects and the approaches being applied.

RE.CNT 228 THERE ARE 228 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:490265 CAPLUS  
 DN 141:52841  
 TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to *M. tuberculosis*, and use thereof as vaccines and in diagnosis  
 IN Andersen, Peter; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter  
 PA Den.  
 SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.  
 CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004115211	A1	20040617	US 2003-620246	20030715
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		

US 1998-50739 A2 19980330  
 DK 1998-1281 A 19981008  
 EP 1998-913536 A3 19980401

**AB** The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

L12 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:80234 CAPLUS

DN 140:144687

TI Molecular differences between species of the *Mycobacterium tuberculosis* complex by genetic deletion markers and genetic marker-encoded antigens

IN Behr, Marcel; Small, Peter; Wilson, Michael A.; Schoolnik, Gary; Aagaard, Claus; Rosenkrands, Ida; Weldingh, Karin; Andersen, Peter

PA Can.

SO U.S. Pat. Appl. Publ., 83 pp., Cont.-in-part of U.S. Ser. No. 894,844.  
 CODEN: USXXCO

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004018574	A1	20040129	US 2003-388902	20030314
	US 6291190	B1	20010918	US 1999-318191	19990525
	US 2002176873	A1	20021128	US 2001-894844	20010627
	US 6686166	B2	20040203		
	US 2004063923	A1	20040401	US 2003-647089	20030821
	WO 2004083448	A2	20040930	WO 2004-US7668	20040311
	WO 2004083448	A3	20060216		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2006002953	A1	20060105	US 2005-143401	20050601
	US 1998-97936P.	P	19980825		
	US 1999-318191	A1	19990525		
	US 2001-894844	A2	20010627		
	US 2003-388902	A	20030314		
	US 2003-647089	B1	20030821		

**AB** Specific genetic deletions are identified that serve as markers to distinguish between avirulent and virulent mycobacteria strains, including *M. bovis*, *M. bovis* BCG strains, *M. tuberculosis* (*M. tb.*) isolates, and bacteriophages that infect mycobacteria. These deletions are used as genetic markers to distinguish between the different mycobacteria. In one embodiment of the invention, a plurality of antigens encoded by the provided genetic markers is used in the diagnosis of *M. tuberculosis* infection. Alternatively, the deleted genes are identified in the *M. tb.* genome sequence, and are then reintroduced by recombinant methods into BCG or other vaccine strains, in order to improve the efficacy of vaccination.

L12 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2004:60336 CAPLUS

DN 140:144681

TI Mycobacterium low oxygen-induced antigens and genes for vaccines or diagnostics of tuberculosis

IN Andersen, Peter; Rosenkrands, Ida; Stryhn, Anette

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 76 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004006952	A2	20040122	WO 2003-DK477	20030708
	WO 2004006952	A3	20040318		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2003242504	A1	20040202	AU 2003-242504	20030708
	EP 1523331	A2	20050420	EP 2003-763613	20030708
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
	US 2004057963	A1	20040325	US 2003-617038	20030711
PRAI	DK 2002-1098	A	20020713		
	US 2002-401725P	P	20020807		
	WO 2003-DK477	W	20030708		

AB The present invention is based on a number of *M. tuberculosis* derived proteins and protein fragments which are induced during the latent stage of infection characterized by low oxygen tension in the microenvironment of the infecting TB-bacteria. The invention is directed to the use of these polypeptides, immunol. active fragments thereof and the genes encoding them for immunol. compns. such as therapeutic vaccines and diagnostic reagents.

L12 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2001:475998 CAPLUS

DN 136:34028

TI Preparation of culture filtrate proteins from *Mycobacterium tuberculosis*

AU Rosenkrands, Ida; Andersen, Peter

CS Department of TB Immunology, Statens Serum Institut, Copenhagen, Den.

SO Methods in Molecular Medicine (2001), 54 (*Mycobacterium tuberculosis Protocols*), 205-215

CODEN: MMMEFN

PB Humana Press Inc.

DT Journal; General Review

LA English

AB A review on the production of culture filtrate suitable for protein identification. Topics covered include culturing *M. tuberculosis* for culture filtrate preparation; culture filtrate analyses; *M. tuberculosis* cultures; harvest of culture filtrate; ultrafiltration and ammonium sulfate precipitation; and protein qualification.

RE.CNT 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2000:260319 CAPLUS

DN 132:292711

TI Tb vaccine and diagnostic based on antigens from the *Mycobacterium tuberculosis* cell

IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rosenkrands, Ida

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 126 pp.  
CODEN: PIXXD2

DT Patent  
LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000021983	A2	20000420	WO 1999-DK538	19991008
	WO 2000021983	A3	20001123		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2346218	AA	20000420	CA 1999-2346218	19991008
	AU 9960784	A1	20000501	AU 1999-60784	19991008
	AU 766093	B2	20031009		
	EP 1117683	A2	20010725	EP 1999-947257	19991008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, IE, SI, LT, LV, FI, RO				

PRAI DK 1998-1281 A 19981008  
US 1999-116673P P 19990121  
WO 1999-DK538 W 19991008

AB The present invention relates to substantially pure polypeptides, which has a sequence identity of at least 80 % to an amino acid sequence disclosed, or which is a subsequence of at least 6 amino acids thereof, preferably a B- or T-cell epitope of the polypeptides disclosed. The polypeptide or the subsequence thereof has at least one of nine properties. The use of the disclosed polypeptides in medicine is disclosed, preferably as vaccine or diagnostic agents relating to virulent **Mycobacterium**. The invention further relates to the nucleotide sequences disclosed and the nucleotide sequences encoding the disclosed polypeptides. Medical and non-medical use of the nucleotide sequences is disclosed.

L12 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1998:684968 CAPLUS

DN 129:300060

TI Novel antigens of **Mycobacterium tuberculosis** culture

IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 264 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	AA	19981008	CA 1998-2285625	19980401
	AU 9868204	A1	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515359	T2	20010918	JP 1998-541074	19980401

EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
CA 2319380	AA	19990520	CA 1998-2319380	19981008
WO 9924577	A1	19990520	WO 1998-DK438	19981008
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1029053	A1	20000823	EP 1998-947412	19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 504951	A	20010629	NZ 1998-504951	19981008
AU 750173	B2	20020711	AU 1998-94338	19981008
EP 1484405	A1	20041208	EP 2004-77071	19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				

PRAI	DK 1997-376	A	19970402
	US 1997-44624P	P	19970418
	DK 1997-1277	A	19971110
	US 1998-70488P	P	19980105
	EP 1998-913536	A3	19980401
	WO 1998-DK132	W	19980401
	EP 1998-947412	A3	19981008
	WO 1998-DK438	W	19981008

AB Culture filtrate antigens of *Mycobacterium tuberculosis* are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12	ANSWER 31 OF 33 USPATFULL on STN
AN	2006:9671 USPATFULL
TI	Compositions and methods for stabilizing lipid based adjuvant formulations using glycolipids
IN	Davidson, Jesper, Solroed Strand, DENMARK Andersen, Peter, Broenshoej, DENMARK Rosenkrands, Ida, Vaerloese, DENMARK
PA	Statens Serum Institut, Copenhagen S, DENMARK (non-U.S. corporation)
PI	US 2006008519 A1 20060112
AI	US 2005-174955 A1 20050705 (11)
PRAI	DK 2004-1070 20040707 US 2004-585908P 20040707 (60)

DT	Utility
FS	APPLICATION
LREP	HOWSON AND HOWSON, ONE SPRING HOUSE CORPORATION CENTER, BOX 457, 321 NORRISTOWN ROAD, SPRING HOUSE, PA, 19477, US
CLMN	Number of Claims: 18
ECL	Exemplary Claim: 1
DRWN	11 Drawing Page(s)

LN.CNT 1191

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to liposome formulations that are physically stable. In particular the present invention relates to steric stabilization of cationic liposomes by incorporating glycolipids into the liposomes. The stabilized liposomes can be used either as an adjuvant for antigenic components or as a drug delivery system. In

particular the invention relates to vaccines with adjuvants in aqueous media for immunization, where the final product is stable.

L12 ANSWER 32 OF 33 USPATFULL on STN  
AN 2004:76186 USPATFULL  
TI Therapeutic TB vaccine  
IN Andersen, Peter, Bronshoj, DENMARK  
Rosenkrands, Ida, Vaerlose, DENMARK  
Stryhn, Anette, Virum, DENMARK  
PI US 2004057963 A1 20040325  
AI US 2003-617038 A1 20030711 (10)  
PRAI DK 2002-1098 20020713  
US 2002-401725P 20020807 (60)  
DT Utility  
FS APPLICATION  
LREP HOWSON AND HOWSON, ONE SPRING HOUSE CORPORATION CENTER, BOX 457, 321 NORRISTOWN ROAD, SPRING HOUSE, PA, 19477  
CLMN Number of Claims: 22  
ECL Exemplary Claim: 1  
DRWN 7 Drawing Page(s)  
LN.CNT 6018

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Therapeutic vaccines comprising polypeptides expressed during the latent stage of **mycobacteria** infection are provided, as are multiphase vaccines, and methods for treating and preventing **tuberculosis**.

L12 ANSWER 33 OF 33 USPATFULL on STN  
AN 2002:178550 USPATFULL  
TI Nucleic acid fragments and polypeptide fragments derived from M. **tuberculosis**  
IN Andersen, Peter, Bronshoj, DENMARK  
Nielsen, Rikke, Frederiksberg C, DENMARK  
Oettinger, Thomas, Hellerup, DENMARK  
Rasmussen, Peter Birk, Copenhagen O, DENMARK  
Rosenkrands, Ida, Copenhagen O, DENMARK  
Weldingh, Karin, Copenhagen N, DENMARK  
Florio, Walter, Frederiksberg C, DENMARK  
PA STATENS SERUM INSTITUT (non-U.S. corporation)  
PI US 2002094336 A1 20020718  
AI US 2001-791171 A1 20010220 (9)  
RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING  
PRAI DK 1997-376 19970402  
DK 1997-1277 19971110  
US 1997-44624P 19970418 (60)  
US 1998-70488P 19980105 (60)  
DT Utility  
FS APPLICATION  
LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151  
CLMN Number of Claims: 53  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Page(s)  
LN.CNT 6134

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is based on the identification and characterization of a number of M. **tuberculosis** derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

E2 3 WELDINGH K N/AU  
E3 50 --> WELDINGH KARIN/AU  
E4 3 WELDINGH KARIN N/AU  
E5 2 WELDINK ERIC/AU  
E6 1 WELDKAMP J F/AU  
E7 1 WELDL C H/AU  
E8 30 WELDLE HELMUT/AU  
E9 1 WELDLER HANS/AU  
E10 1 WELDLICH C/AU  
E11 1 WELDLICH O/AU  
E12 1 WELDLICH U/AU

=> s e1-e4 and mycobact?

L13 108 ("WELDINGH K"/AU OR "WELDINGH K N"/AU OR "WELDINGH KARIN"/AU OR "WELDINGH KARIN N"/AU) AND MYCOBACT?

=> dup rem 113

PROCESSING COMPLETED FOR L13

L14 29 DUP REM L13 (79 DUPLICATES REMOVED)

=> d bib ab 1-

YOU HAVE REQUESTED DATA FROM 29 ANSWERS - CONTINUE? Y/(N):y

L14 ANSWER 1 OF 29 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 1  
AN 2006126612 EMBASE  
TI Use of enzyme-linked immunospot assay with **Mycobacterium** tuberculosis-specific peptides for diagnosis of recent infection with *M. tuberculosis* after accidental laboratory exposure.  
AU Leyten E.M.S.; Mulder B.; Prins C.; Weldingh K.; Andersen P.; Ottenhoff T.H.M.; Van Dissel J.T.; Arend S.M.  
CS E.M.S. Leyten, Dept. of Infectious Diseases, Leiden University Medical Center, P.O. Box 9600, 2300 RC Leiden, Netherlands. e.m.s.leyten@LUMC.nl  
SO Journal of Clinical Microbiology, (2006) Vol. 44, No. 3, pp. 1197-1201. .  
Refs: 31  
ISSN: 0095-1137 CODEN: JCMIDW  
CY United States  
DT Journal; Article  
FS 004 Microbiology  
017 Public Health, Social Medicine and Epidemiology  
035 Occupational Health and Industrial Medicine  
LA English  
SL English  
ED Entered STN: 31 Mar 2006  
Last Updated on STN: 31 Mar 2006  
AB This report of an accidental exposure to **Mycobacterium** tuberculosis in a microbiological laboratory illustrates the value of gamma interferon enzyme-linked immunospot assay using peptides of ESAT-6, CFP-10, TB37.6, and TB7.7 for the diagnosis of latent infection. In particular, positive responses to peptides 2 to 6 of TB37.6 were observed exclusively in recently infected persons. Copyright .COPYRGT. 2006, American Society for Microbiology. All Rights Reserved.

L14 ANSWER 2 OF 29 CABAB COPYRIGHT 2006 CABI on STN DUPLICATE 2

AN 2006:68095 CABAB

DN 20063053675

TI Prospects for a novel vaccine against tuberculosis

AU Dietrich, J.; Weldingh, K.; Andersen, P.; More, S. J. [EDITOR]; Collins, J. D. [EDITOR]; Gormley, E. [EDITOR]; Good, M. [EDITOR]; Skuce, R. A. [EDITOR]; Pollock, J. M. [EDITOR]

CS Department of Infectious Disease Immunology, Statens Serum Institute, Artillerivej 5, 2300 Copenhagen S, Denmark. jdi@ssi.dk

SO Veterinary Microbiology, (2006) Vol. 112, No. 2/4, pp. 163-169. many ref.

Publisher: Elsevier. Amsterdam

Price: Journal article; Conference paper .

Meeting Info.: Proceedings of the 4th International Conference on Mycobacterium bovis, Dublin, Ireland, 22-26 August 2005.

ISSN: 0378-1135

CY Netherlands Antilles  
DT Journal  
LA English  
ED Entered STN: 5 Apr 2006  
Last Updated on STN: 5 Apr 2006  
AB The development of a new and improved vaccine against tuberculosis has in the last 10 years been accelerated tremendously from the completed *Mycobacterium tuberculosis* genome and the progress in molecular biology. This has resulted in the identification of a large number of antigens with potential in tuberculosis vaccines. The next phase of this work has now started - putting the most relevant molecules back together as fusion molecules and cocktails. This requires carefully monitoring of aspects as immunodominance, recognition in different populations as well as the influence of different adjuvants and delivery systems. The most advanced of these vaccines such as the fusion between ESAT6 and Ag85B have been evaluated in a range of animal models including non-human primates and are now entering into clinical trials. For these vaccines to be successfully implemented in future vaccination programmes it is necessary to understand the immunological background for the failure of BCG and optimize the vaccines for their ability to boost the immuneresponse primed by BCG.

L14 ANSWER 3 OF 29 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN DUPLICATE 3  
AN 2005377026 EMBASE  
TI [A possible successor to the Mantoux test after 97 years].  
EN MULIG AFLØSER TIL MANTOUXTEST EFTER 97 AR.  
AU Ravn P.; Brock I.; Andersen P.; Weldingh K.  
SO Ugeskrift for Laeger, (8 Aug 2005) Vol. 167, No. 32, pp. 2905-2906. .  
Refs: 5  
ISSN: 0041-5782 CODEN: UGLAAD  
CY Denmark  
DT Journal; (Short Survey)  
FS 004 Microbiology  
015 Chest Diseases, Thoracic Surgery and Tuberculosis  
026 Immunology, Serology and Transplantation  
LA Danish  
ED Entered STN: 15 Sep 2005  
Last Updated on STN: 15 Sep 2005

L14 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4  
AN 2005:1168451 CAPLUS  
TI Replacing the tuberculin skin test with a specific blood test  
AU Weldingh, Karin; Andersen, Peter  
CS Department of Infectious Disease Immunology, Statens Serum Institute, Copenhagen, 2300, Den.  
SO Kekkaku (2005), 80(8), 581-585  
CODEN: KEKKAG; ISSN: 0022-9776  
PB Nippon Kekkakubyo Gakkai  
DT Journal  
LA English  
AB For almost 100 years has the tuberculin skin test (TST) been used for the support the diagnosis of active and latent TB infection. The TST test has, however, a number of limitations most notable low specificity in BCG vaccinated individuals due to cross-reactive components in PPD and the *M. bovis* BCG vaccine strain and an intensive search for new and more specific diagnostic antigens has therefore be ongoing. In this review we describe the discovery process leading to the identification of the *M. tuberculosis* specific antigens ESAT6 and CFPI0; two low mol. weight proteins which are highly sensitive and specific for detection of a *M. tuberculosis* infection.

RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 5  
AN 2005:464789 BIOSIS  
DN PREV200510248324  
TI Prospective evaluation of a whole-blood test using *Mycobacterium*

tuberculosis-specific antigens ESAT-6 and CFP-10 for diagnosis of active tuberculosis.

AU Ravn, Pernille [Reprint Author]; Munk, Martin E.; Andersen, Ase B.; Lundgren, Bettina; Lundgren, Jens D.; Nielsen, Lars N.; Kok-Jensen, Axel; Andersen, Peter; Weldingh, Karin  
CS Hvidovre Hosp, Dept Infect Dis, Kettegards Alle 30, DK-2650 Hvidovre, Denmark  
pravn@dadlnet.dk  
SO Clinical and Diagnostic Laboratory Immunology, (APR 2005) Vol. 12, No. 4, pp. 491-496.  
ISSN: 1071-412X.

DT Article  
LA English  
ED Entered STN: 9 Nov 2005  
Last Updated on STN: 9 Nov 2005

AB A new immunodiagnostic test based on the **Mycobacterium** tuberculosis-specific antigens CFP-10/ESAT-6(QFT-RD1) has been launched as an aid in the diagnosis of latent tuberculosis (TB) infection (LTBI). The aim of this study was to evaluate this test for the diagnosis of active TB. Eighty-two patients with suspicion of TB and 39 healthy BCG-vaccinated persons were enrolled. Forty-eight had active TB, 25 did not, and 9 were excluded. Sensitivity and specificity of the test for active TB were evaluated in a prospective blinded manner in patients suspected of TB. The sensitivity of the QFT-RDI was 85 % (40/48; confidence interval [CI], 75 to 96), and it was higher than the sensitivity of microscopy, 42 % (20/48; CI, 27 to 56; P = 0.001), and culture, 59 % (27/46; CI, 44 to 73; P = 0.009). Of patients with extrapulmonary TB, 92 % (12/13) were QFT-RDI positive, whereas only 31 % (4/13) were positive by microscopy and 42 % (5/12) by culture (P < 0.05), and 87 % (13/15) of those who were negative by both microscopy and culture were QFT-RDI positive. By combining microscopy and culture with the QFT-RDI test, sensitivity increased to 96 % (CI, 90 to 102). Ten of 25 (40 %) non-TB patients were QFT-RDI positive, resulting in a specificity of 60 %. However, 80 % (8/10) of these had risk-factors for TB, indicating latent infection in this group. In healthy controls, only 3 % (1/39) were QFT-RDI positive. In conclusion, the QFT-RDI test is sensitive for diagnosis of TB, especially in patients with negative microscopy and culture. The accuracy of the QFT-RDI test will vary with the prevalence of LTBI. We suggest that the QFT-RDI test could be a very useful supplementary tool for the diagnosis of TB.

L14 ANSWER 6 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
AN 2006:6103 BIOSIS  
DN PREV200600003616  
TI Inhibition of anti-tuberculosis effector T lymphocytes with tumor necrosis factor antagonist treatment.

AU Mariette, Xavier [Reprint Author]; Hamdi, Haifa; Weldingh, Karin ; Puechal, Xavier; Breban, Maxime; Berenbaum, Francis; Flipo, Rene Marc; Meyer, Olivier; Falgarone, Geraldine; Liote, Frederic; Claudepierre, Pascal; Lemann, Marc; Humbert, Marc; Salmon, Dominique; Emilie, Dominique; Club Rhumatismes Inflammation [Reprint Author]

CS Bicetre Hosp, Le Kremlin Bicetre, France

SO Arthritis & Rheumatism, (SEP 2005) Vol. 52, No. 9, Suppl. S, pp. S338. Meeting Info.: 69th Annual Scientific Meeting of the American-College-of-Rheumatology/40th Annual Scientific Meeting of the Association-of-Rheumatology-Health-Professionals. San Diego, CA, USA. November 12 -17, 2005. Amer Coll Rheumatol; Assoc Rheumatol Hlth Profess. CODEN: ARHEAW. ISSN: 0004-3591.

DT Conference; (Meeting)  
Conference; Abstract; (Meeting Abstract)

LA English

ED Entered STN: 14 Dec 2005

Last Updated on STN: 14 Dec 2005

L14 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6  
AN 2005:119461 CAPLUS  
DN 142:334537

TI Assessing the serodiagnostic potential of 35 **Mycobacterium** tuberculosis proteins and identification of four novel serological

AU antigens  
Weldingh, Karin; Rosenkrands, Ida; Okkels, Limei Meng; Doherty, T. Mark; Andersen, Peter  
CS Department of Infectious Disease Immunology, Statens Serum Institut, Copenhagen, Den.  
SO Journal of Clinical Microbiology (2005), 43(1), 57-65  
CODEN: JCMIDW; ISSN: 0095-1137  
PB American Society for Microbiology  
DT Journal  
LA English  
AB Improved diagnostic reagents are needed for the detection of *Mycobacterium tuberculosis* infections, and the development of a serodiagnostic test would complement presently available diagnostic methods. The aim of the present study was to identify novel serol. targets for use for the future serodiagnosis of tuberculosis (TB). The authors cloned and expressed 35 *M. tuberculosis* proteins as recombinant proteins in *Escherichia coli* and analyzed their serodiagnostic potentials. By a two-step selection process, four superior seroantigens, TB9.7, TB15.3, TB16.3, and TB51, were identified, none of which has been described before. The four novel antigens were tested with panels of sera from smear-pos. and smear-neg. TB patients from areas both where TB is endemic and where TB is not endemic, with recognition frequencies ranging from 31 to 93% and with a specificity of at least 97%. The single most potent antigen was TB16.3, which had a sensitivity of 48 to 55% with samples from Danish resident TB patients and a sensitivity of 88 to 98% with samples from African TB patients. Importantly, the TB16.3 and the TB9.7 antigens were recognized by more than 85% of the samples from TB patients coinfected with human immunodeficiency virus, a patient group for which it is in general difficult to detect *M. tuberculosis*-specific antibodies.

RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7  
AN 2004:490265 CAPLUS  
DN 141:52841  
TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to *M. tuberculosis*, and use thereof as vaccines and in diagnosis  
IN Andersen, Peter; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter  
PA Den.  
SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
PI US 2004115211	A1	20040617	US 2003-620246	20030715
US 6641814	B1	20031104	US 1998-50739	19980330
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI DK 1997-376	A	19970402		
US 1997-44624P	P	19970418		
DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
US 1998-50739	A2	19980330		
DK 1998-1281	A	19981008		
EP 1998-913536	A3	19980401		
AB The present invention is based on the identification and characterization of a number of <i>M. tuberculosis</i> derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between				

ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

L14 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8  
AN 2004:80234 CAPLUS  
DN 140:144687  
TI Molecular differences between species of the **Mycobacterium** tuberculosis complex by genetic deletion markers and genetic marker-encoded antigens  
IN Behr, Marcel; Small, Peter; Wilson, Michael A.; Schoolnik, Gary; Aagaard, Claus; Rosenkrands, Ida; Weldingh, Karin; Andersen, Peter  
PA Can.  
SO U.S. Pat. Appl. Publ., 83 pp., Cont.-in-part of U.S. Ser. No. 894,844.  
CODEN: USXXCO  
DT Patent  
LA English  
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----
PI US 2004018574	A1	20040129	US 2003-388902	20030314
US 6291190	B1	20010918	US 1999-318191	19990525
US 2002176873	A1	20021128	US 2001-894844	20010627
US 6686166	B2	20040203		
US 2004063923	A1	20040401	US 2003-647089	20030821
WO 2004083448	A2	20040930	WO 2004-US7668	20040311
WO 2004083448	A3	20060216		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006002953	A1	20060105	US 2005-143401	20050601
PRAI US 1998-97936P	P	19980825		
US 1999-318191	A1	19990525		
US 2001-894844	A2	20010627		
US 2003-388902	A	20030314		
US 2003-647089	B1	20030821		
AB Specific genetic deletions are identified that serve as markers to distinguish between avirulent and virulent <b>mycobacteria</b> strains, including <i>M. bovis</i> , <i>M. bovis</i> BCG strains, <i>M. tuberculosis</i> ( <i>M. tb.</i> ) isolates, and bacteriophages that infect <b>mycobacteria</b> . These deletions are used as genetic markers to distinguish between the different <b>mycobacteria</b> . In one embodiment of the invention, a plurality of antigens encoded by the provided genetic markers is used in the diagnosis of <i>M. tuberculosis</i> infection. Alternatively, the deleted genes are identified in the <i>M. tb.</i> genome sequence, and are then reintroduced by recombinant methods into BCG or other vaccine strains, in order to improve the efficacy of vaccination.				

L14 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 2004:996402 CAPLUS  
DN 141:423306  
TI Compositions comprising multiple T cell epitopes of **mycobacterial** antigens for immunodiagnosis and immunotherapy of tuberculosis  
IN Andersen, Peter; Brock, Inger; Weldingh, Karin  
PA Statens Serum Institut, Den.  
SO PCT Int. Appl., 65 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	-----	-----	-----	-----

PI	WO 2004099771	A1	20041118	WO 2004-DK314	20040506
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRAI DK 2003-699 A 20030508

AB The current used method for immunol. diagnosis of tuberculosis infection, the tuberculin skin test, is problematic for a number of reasons; it has low specificity in BCG vaccinated individuals, a high interobserver variance and requires skill to be read and interpreted. Furthermore it requires an extra visit to the clinic to have the test read. Both people vaccinated with BCG and those exposed to non-tuberculosis **mycobacteria** give a pos. skin test result similar to that seen in a TB infected individual. This also applies for purified protein derivative (PPD) when used in a blood cell based test. The present invention disclosed the development of an immunol. TB diagnostic tool based on a combination of T cell epitopes from proteins encoded by regions of the *M. tuberculosis* genome, that are not present in the BCG vaccine strain or in the most common non-tuberculosis **mycobacteria**. Four recently characterized proteins (i.e. Rv2654, Rv2653, Rv3873 and Rv3878) with this diagnostic potential were selected. Peptides from these proteins were tested one by one with peripheral blood mononuclear cells from microscopy or culture confirmed TB patients as well as from healthy BCG vaccinated controls. Some combinations of peptides showed a sensitivity level comparable to the level seen with these peptides combined with ESAT 6 and CFP 10 gave a sensitivity of 93% representing a raise in sensitivity of about 26-33% compared to using ESAT6 or CFP10 alone. The results from a panel of TB patients, using a collection of the new specific epitopes clearly demonstrates, the addition of other specific epitopes to the already known specific antigens, increases the sensitivity of a diagnostic assay based on cell mediated immune response.

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 11 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 9

AN 2004:309660 BIOSIS

DN PREV200400309678

TI Healthy individuals that control a latent infection with **Mycobacterium** tuberculosis express high levels of Th1 cytokines and the IL-4 antagonist IL-4delta2.

AU Demissie, Abebech; Abebe, Markos; Aseffa, Abraham; Rook, Graham; Fletcher, Helen; Zumla, Alimuddin; Weldingh, Karin; Brock, Inger; Andersen, Peter; Doherty, T. Mark [Reprint Author]; VACSEL Study Group

CS Dept Infect Dis Immunol, Statens Serum Inst, Artillerivej 5, DK-2300, Copenhagen, S, Denmark  
TMD@ssi.dk

SO Journal of Immunology, (June 1 2004) Vol. 172, No. 11, pp. 6938-6943.  
print.  
ISSN: 0022-1767 (ISSN print).

DT Article

LA English

ED Entered STN: 7 Jul 2004  
Last Updated on STN: 7 Jul 2004

AB The majority of healthy individuals exposed to **Mycobacterium** tuberculosis will not develop disease and identifying what constitutes "protective immunity" is one of the holy grails of *M. tuberculosis* immunology. It is known that IFN-gamma is essential for protection, but it is also apparent that IFN-gamma levels alone do not explain the immunity/susceptibility dichotomy. The controversy regarding correlates of immunity persists because identifying infected but healthy individuals

(those who are immune) has been problematic. We have therefore used recognition of the *M. tuberculosis* virulence factor early secretory antigenic target 6 to identify healthy, but infected individuals from tuberculosis (TB)-endemic and nonendemic regions (Ethiopia and Denmark) and have compared signals for cytokines expressed directly ex vivo with the pattern found in TB patients. We find that TB patients are characterized by decreased levels of Th1 cytokines and increased levels of IL-10 compared with the healthy infected and noninfected community controls. Interestingly, the healthy infected subjects exhibited a selective increase of message for the IL-4 antagonist, IL-4delta2, compared with both TB patients or noninfected individuals. These data suggest that long-term control of *M. tuberculosis* infection is associated not just with elevated Th1 responses but also with inhibition of the Th2 response.

L14 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 10  
AN 2004:572566 CAPLUS  
DN 141:294300  
TI Specific T-cell epitopes for immunoassay-based diagnosis of *Mycobacterium tuberculosis* infection  
AU Brock, Inger; Weldingh, Karin; Leyten, Eliane M. S.; Arend, Sandra M.; Ravn, Pernille; Andersen, Peter  
CS Department of Infectious Disease Immunology, Statens Serum Institute, Copenhagen, Den.  
SO Journal of Clinical Microbiology (2004), 42(6), 2379-2387  
CODEN: JCMIDW; ISSN: 0095-1137  
PB American Society for Microbiology  
DT Journal  
LA English  
AB The currently used method for immunol. detection of tuberculosis infection, the tuberculin skin test, has low specificity. Antigens specific for *Mycobacterium tuberculosis* to replace purified protein derivative are therefore urgently needed. We have performed a rigorous assessment of the diagnostic potential of four recently identified antigens (Rv2653, Rv2654, Rv3873, and Rv3878) from genomic regions that are lacking from the *Mycobacterium bovis* bacillus Calmette-Guerin (BCG) vaccine strains as well as from the most common nontuberculous mycobacteria. The fine specificity of potential epitopes in these mols. was evaluated by sensitive testing of the T-cell responses of peripheral blood mononuclear cells derived from *M. bovis* BCG-vaccinated healthy individuals to synthesized overlapping peptides. Three of the four mols. contained regions with significant specificity problems (Rv2653, Rv3873, and Rv3878). We selected and combined the specific peptide stretches from the four proteins not recognized by *M. bovis* BCG-vaccinated individuals. These peptide stretches were tested with peripheral blood mononuclear cells obtained from patients with microscopy-or culture-confirmed tuberculosis and from healthy *M. bovis* BCG-vaccinated controls. The combination of the most promising stretches from this anal. showed a sensitivity level (57%) comparable to the level found with the two well-known *M. tuberculosis*-specific proteins ESAT-6 and CFP-10 (75 and 66%, resp.). The combination of ESAT-6, CFP-10, and the novel specific peptide stretches gave an overall sensitivity of 84% at a specificity of 97%. In a validation experiment with new exptl. groups, the sensitivities obtained were 57% for the combination of peptides and 90% for the combination of the peptides, ESAT-6, and CFP-10. This combination gave a specificity of 95%.

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 13 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 11  
AN 2004:211482 BIOSIS  
DN PREV200400213609  
TI Mapping immune reactivity toward Rv2653 and Rv2654: Two novel low-molecular-mass antigens found specifically in the *Mycobacterium tuberculosis* complex.  
AU Aagaard, Claus [Reprint Author]; Brock, Inger; Olsen, Anja; Ottenhoff, Tom H. M.; Weldingh, Karin; Andersen, Peter  
CS Dept. of Infectious Disease Immunology, Statens Serum Institute,

Artillerivej 5, DK-2300, Copenhagen, Denmark  
caa@ssi.dk

SO Journal of Infectious Diseases, (1 March 2004) Vol. 189, No. 5, pp.  
812-819. print.  
CODEN: JIDIAQ. ISSN: 0022-1899.

DT Article

LA English

ED Entered STN: 14 Apr 2004

Last Updated on STN: 14 Apr 2004

AB New tools are urgently needed for the detection of latent tuberculosis (TB). We evaluated the diagnostic potential of 2 novel *Mycobacterium tuberculosis* complex-specific candidate antigens (Rv2653 and Rv2654) and investigated T cell recognition during natural infection in humans and experimental infection in guinea pigs. Peripheral blood mononuclear cells stimulated with peptide pools covering the full length of Rv2654 induced interferon-gamma release in 10 of 19 patients with TB. Neither Rv2654 single peptides nor Rv2654 pools were recognized by bacille Calmette-Guerin-vaccinated donors. However, peptides from Rv2653 were recognized by both patients group. The cross-reactive epitope(s) in Rv2653 were located in a 36-amino acid stretch in the center of the molecule. Rv2654 also induced *M. tuberculosis*-specific skin-test responses in 3 of 4 aerosol-infected guinea pigs. Rv2654 is a strongly recognized T cell antigen that is highly specific for TB and has potential as a novel cell-mediated immunity-based TB diagnostic agent.

L14 ANSWER 14 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 12

AN 2004:345624 BIOSIS

DN PREV200400347773

TI Reactivation of tuberculosis during immunosuppressive treatment in a patient with a positive QuantiFERON(R)-RD1 Test.

AU Ravn, Pernille [Reprint Author]; Munk, Martin E.; Andersen, Ase Bengaard; Lundgren, Bettina; Nielsen, Lars N.; Lillebaek, Troels; Soerensen, Inge J.; Andersen, Peter; Weldingh, Karin

CS Hvidovre HospDept Infect Dis, Univ Copenhagen, Kettegards Alle 30, DK-2650, Hvidovre, Denmark

pravn@dadlnet.dk

SO Scandinavian Journal of Infectious Diseases, (July 2004) Vol. 36, No. 6-7, pp. 499-501, 497. print.

CODEN: SJIDB7. ISSN: 0036-5548.

DT Article

LA English

ED Entered STN: 18 Aug 2004

Last Updated on STN: 18 Aug 2004

AB A patient with polymyositis developed tuberculosis during immunosuppressive treatment. Tuberculin Skin Test and chest X-ray failed to demonstrate latent tuberculosis, whereas a blood sample that was tested with a modified QuantiFERON(R)-TB-assay, using the recombinant ESAT-6 and CFP-10, was positive indicating that this patient was latently infected before immunosuppressive therapy. This case indicates the risk of progressing from latent to active tuberculosis given that the subject is RD1 responsive, and we believe that preventive anti-tuberculous treatment could have prevented this case of tuberculosis. We suggest that RD1 based tests are evaluated further in immunocompromised patients.

L14 ANSWER 15 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 13

AN 2004:340175 BIOSIS

DN PREV200400343460

TI Comparison of tuberculin skin test and new specific blood test in tuberculosis contacts.

AU Brock, Iinger; Weldingh, Karin; Lillebaek, Troels; Follmann, Frank; Andersen, Peter [Reprint Author]

CS Dept Infect Dis Immunol, Statens Serum Inst, Artillerivej 5, DK-2300, Copenhagen, Denmark

pa@ssi.dk

SO American Journal of Respiratory and Critical Care Medicine, (July 1 2004) Vol. 170, No. 1, pp. 65-69. print.

ISSN: 1073-449X (ISSN print).

DT Article  
LA English  
ED Entered STN: 11 Aug 2004  
Last Updated on STN: 11 Aug 2004  
AB The tuberculin skin test used to detect latent **Mycobacterium** tuberculosis infection has many drawbacks, and a new diagnostic test for latent tuberculosis (QuantiFERON-TB (QTF-TB)) has recently been introduced. This test measures the production of IFN-gamma in whole blood upon stimulation with purified protein derivative (PPD). The QTF-TB test addresses the operational problems with the tuberculin skin test, but, as the test is based on PPD, it still has a low specificity in populations vaccinated with the Bacille Calmette-Guerin (BCG) vaccine. We have modified the test to include the antigens ESAT-6 and CFP-10, which are not present in BCG vaccine strains or the vast majority of nontuberculous mycobacteria. This test was used to detect infection in contacts in a tuberculosis outbreak at a Danish high school. The majority of the contacts were BCG-unvaccinated, which allowed a direct comparison of the skin test and the novel blood test in individuals whose skin test was not confounded by vaccination. An excellent agreement between the two tests was found (94%, kappa value 0.866), and in contrast to the blood test based on PPD, the novel blood test was not influenced by the vaccination status of the subjects tested.

L14 ANSWER 16 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN DUPLICATE 14

AN 2004:5335 BIOSIS

DN PREV200400007544

TI Nucleic acids fragments and polypeptide fragments derived from M. tuberculosis.

AU Andersen, Peter [Inventor, Reprint Author]; Nielsen, Rikke [Inventor]; Oettinger, Thomas [Inventor]; Rasmussen, Peter Birk [Inventor]; Rosenkrands, Ida [Inventor]; Weldingh, Karin [Inventor]; Florio, Walter [Inventor]

CS Bronshoj, Denmark

ASSIGNEE: Statens Serum Institut, Copenhagen, Denmark

PI US 6641814 20031104

SO Official Gazette of the United States Patent and Trademark Office Patents, (Nov 4 2003) Vol. 1276, No. 1. <http://www.uspto.gov/web/menu/patdata.html>. e-file.

ISSN: 0098-1133 (ISSN print).

DT Patent

LA English

ED Entered STN: 17 Dec 2003

Last Updated on STN: 17 Dec 2003

AB The present invention is based on the identification and characterization of a number of M. tuberculosis derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L14 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 15

AN 2003:696302 CAPLUS

DN 139:229237

TI Protein and DNA sequences of antigens from **Mycobacterium** and uses in tuberculosis diagnosis and treatment

IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Vegerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk

PA Statens Serum Institut, Den.

SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.

CODEN: USXXCO

DT Patent

LA English

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6982085	B2	20060103		
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, FI, CY

PRAI	US 2002094336	A1	20020718	US 2001-791171	20010220
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	US 2001-791171	B2	20010220		
	US 2002-60428	A2	20020129		
	EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from **Mycobacterium tuberculosis**. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing tuberculosis caused by virulent **mycobacteria**, e.g. by **Mycobacterium tuberculosis**, **Mycobacterium africanum** or **Mycobacterium bovis**, in an animal, including a human being. The invention related to treating tuberculosis using antigens isolated from **Mycobacterium tuberculosis**.

L14 ANSWER 18 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 16

AN 2004:76163 BIOSIS

DN PREV200400078267

TI Human T-cell responses to the RD1-encoded protein TB27.4 (Rv3878) from **Mycobacterium tuberculosis**.

AU Agger, Else Marie [Reprint Author]; Brock, Inger; Okkels, Limei Meng;  
Arend, Sandra M.; Aagaard, Claus S.; Weldingh, Karin N.;  
Andersen, Peter

CS Department of Infectious Disease Immunology, Statens Serum Institut,  
Artillerivej 5, DK-2300, Copenhagen, S, Denmark  
eag@ssi.dk

SO Immunology, (December 2003) Vol. 110, No. 4, pp. 507-512. print.  
CODEN: IMMUAM. ISSN: 0019-2805.

DT Article

LA English

ED Entered STN: 4 Feb 2004

Last Updated on STN: 4 Feb 2004

AB In recent years, there has been considerable focus on the discovery and characterization of proteins derived from **Mycobacterium tuberculosis** leading to the identification of a number of candidate antigens for use in vaccine development or for diagnostic purposes. Previous experiments have demonstrated an important immunological role for proteins encoded by the RD1 region, which is absent from all strains of bacillus Calmette-Guerin (BCG) but present in the genomes of virulent *M. bovis* and *M. tuberculosis*. Herein, we have studied human T-cell responses to the antigen encoded by the putative open reading frame (rv3878) of the RD1 region. Immunoblot analysis revealed that rv3878 was expressed and the native protein was designated TB27.4. Immunological evaluations demonstrate that TB27.4 elicits a prominent immune response in human tuberculosis patients with a dominant region in the C-terminal part of the molecule. In contrast, very limited responses were seen in *M. bovis* BCG-vaccinated donors. This study therefore emphasizes the diagnostic potential of proteins encoded by the RD1 region.

L14 ANSWER 19 OF 29 USPATFULL on STN

AN 2002:178550 USPATEFULL  
TI Nucleic acid fragments and polypeptide fragments derived from M.  
tuberculosis  
IN Andersen, Peter, Bronshoj, DENMARK  
Nielsen, Rikke, Frederiksberg C, DENMARK  
Oettinger, Thomas, Hellerup, DENMARK  
Rasmussen, Peter Birk, Kobenhaven O, DENMARK  
Rosenkrands, Ida, Kobenhaven O, DENMARK  
Weldingh, Karin, Kobenhaven N, DENMARK  
Florio, Walter, Frederiksberg C, DENMARK  
PA STATENS SERUM INSTITUT (non-U.S. corporation)  
PI US 2002094336 A1 20020718  
AI US 2001-791171 A1 20010220 (9)  
RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING  
PRAI DK 1997-376 19970402  
DK 1997-1277 19971110  
US 1997-44624P 19970418 (60)  
US 1998-70488P 19980105 (60)  
DT Utility  
FS APPLICATION  
LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151  
CLMN Number of Claims: 53  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Page(s)  
LN.CNT 6134  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L14 ANSWER 20 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 17

AN 2003:34905 BIOSIS  
DN PREV200300034905  
TI Specific acquired resistance in mice immunized with killed  
**mycobacteria**.  
AU Agger, E. M.; Weldingh, K.; Olsen, A. W.; Rosenkrands, I.;  
Andersen, P. [Reprint Author]  
CS Department of TB Immunology, Statens Serum Institut, Artillerivej 5,  
DK-2300, Copenhagen, Denmark  
pa@ssi.dk  
SO Scandinavian Journal of Immunology, (November 2002) Vol. 56, No. 5, pp.  
443-447. print.  
ISSN: 0300-9475 (ISSN print).  
DT Article  
LA English  
ED Entered STN: 8 Jan 2003  
Last Updated on STN: 8 Jan 2003  
AB Past attempts to raise resistance against *Mycobacterium*  
tuberculosis using various preparations of killed **mycobacteria**  
have questioned the specificity of the generated immune response. In the  
present study, we have focused on the protective efficacy of experimental  
vaccines based on killed **mycobacteria**. We demonstrate that  
killed **mycobacteria** can confer high levels of protection, which  
can be adoptively transferred to recipient T-cell-deficient mice.  
Moreover, protective antigens can be found in the cell wall, membrane and  
cytosol of the **mycobacterial** cell, and hence emphasize the  
importance of searching for protective antigens in various compartments of  
the **mycobacterial** cell.

AN 2001:780953 CAPLUS  
 DN 135:343273  
 TI Cloning and immunogenicity of **Mycobacterium tuberculosis** proteins  
 IN Agger, Else Marie; Andersen, Peter; Okkels, Li Mei Meng; Weldingh, Karin  
 PA Statens Serum Institut, Den.  
 SO PCT Int. Appl., 111 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001079274	A2	20011025	WO 2001-DK276	20010419
WO 2001079274	A3	20020711		
WO 2001079274	B1	20020808		
WO 2001079274	C1	20040429		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2405247	AA	20011025	CA 2001-2405247	20010419
EP 1278769	A2	20030129	EP 2001-923542	20010419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRAI DK 2000-666	A	20000419		
DK 2001-283	A	20010221		
WO 2001-DK276	W	20010419		

AB The authors disclose the identification and characterization of a number of novel **Mycobacterium tuberculosis** derived proteins and protein fragments. The proteins and protein fragments were examined for their ability to elicit interferon- $\gamma$  production and/or a T-cell proliferative response in guinea pigs and humans with tuberculosis.

L14 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN  
 AN 2000:260319 CAPLUS  
 DN 132:292711  
 TI Tb vaccine and diagnostic based on antigens from the **Mycobacterium tuberculosis** cell  
 IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Vegerby;  
Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther;  
Rosenkrands, Ida  
 PA Statens Serum Institut, Den.  
 SO PCT Int. Appl., 126 pp.  
 CODEN: PIXXD2

DT Patent  
 LA English  
 FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000021983	A2	20000420	WO 1999-DK538	19991008
WO 2000021983	A3	20001123		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2346218	AA	20000420	CA 1999-2346218	19991008
AU 9960784	A1	20000501	AU 1999-60784	19991008

AU 766093 B2 20031009  
EP 1117683 A2 20010725 EP 1999-947257 19991008  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, IE, SI, LT, LV,  
FI, RO  
PRAI DK 1998-1281 A 19981008  
US 1999-116673P P 19990121  
WO 1999-DK538 W 19991008

AB The present invention relates to substantially pure polypeptides, which has a sequence identity of at least 80 % to an amino acid sequence disclosed, or which is a subsequence of at least 6 amino acids thereof, preferably a B- or T-cell epitope of the polypeptides disclosed. The polypeptide or the subsequence thereof has at least one of nine properties. The use of the disclosed polypeptides in medicine is disclosed, preferably as vaccine or diagnostic agents relating to virulent *Mycobacterium*. The invention further relates to the nucleotide sequences disclosed and the nucleotide sequences encoding the disclosed polypeptides. Medical and non-medical use of the nucleotide sequences is disclosed.

L14 ANSWER 23 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 18

AN 2001:37127 BIOSIS

DN PREV200100037127

TI Towards the proteome of *Mycobacterium tuberculosis*.

AU Rosenkrands, Ida [Reprint author]; King, Angus; Weldingh, Karin;  
Moniatte, Marc; Moertz, Ejvind; Andersen, Peter

CS Department of TB Immunology, Statens Serum Institut, 5 Artillerivej,  
DK-2300, Copenhagen S, Denmark  
idr@ssi.dk

SO Electrophoresis, (November, 2000) Vol. 21, No. 17, pp. 3740-3756. print.  
CODEN: ELCTDN. ISSN: 0173-0835.

DT Article

LA English

ED Entered STN: 17 Jan 2001

Last Updated on STN: 12 Feb 2002

AB Human tuberculosis is caused by the intracellular pathogen *Mycobacterium tuberculosis*. Sequencing of the genome of *M. tuberculosis* strain H37Rv has predicted 3924 open reading frames, and enabled identification of proteins from this bacterium by peptide mass fingerprinting. Extracellular proteins from the culture medium and proteins in cellular extracts were examined by two-dimensional gel electrophoresis using immobilized pH gradient technology. By mass spectrometry and immunodetection, 49 culture filtrate proteins and 118 lysate proteins were identified, 83 of which were novel. To date, 288 proteins have been identified in *M. tuberculosis* proteome studies, and a list is presented which includes all identified proteins (available at <http://www.ssi.dk/publichealth/tbimmun>). The information obtained from the *M. tuberculosis* proteome so far is discussed in relation to the information obtained from the complete genome sequence.

L14 ANSWER 24 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 19

AN 2000:271567 BIOSIS

DN PREV200000271567

TI Mapping and identification of *Mycobacterium tuberculosis* proteins by two-dimensional gel electrophoresis, microsequencing and immunodetection.

AU Rosenkrands, Ida; Weldingh, Karin; Jacobsen, Susanne; Hansen,  
Christina Vegerby; Florio, Walter; Gianetri, Isabella; Andersen, Peter  
[Reprint author]

CS Department of TB Immunology, Statens Serum Institute, 5 Artillerivej,  
DK-2300, Copenhagen S, Denmark

SO Electrophoresis, (March, 2000) Vol. 21, No. 5, pp. 935-948. print.  
CODEN: ELCTDN. ISSN: 0173-0835.

DT Article

LA English

ED Entered STN: 30 Jun 2000

Last Updated on STN: 5 Jan 2002

AB *Mycobacterium tuberculosis* is the infectious agent giving rise

to human tuberculosis. The entire genome of *M. tuberculosis*, comprising approximately 4000 open reading frames, has been sequenced. The huge amount of information released from this project has facilitated proteome analysis of *M. tuberculosis*. Two-dimensional polyacrylamide gel electrophoresis (2-D PAGE) was applied to fractions derived from *M. tuberculosis* culture filtrate, cell wall, and cytosol, resulting in the resolution of 376, 413, and 395 spots, respectively, in silver-stained gels. By microsequencing and immunodetection, 38 culture filtrate proteins were identified and mapped, of which 12 were identified for the first time. In the same manner, 23 cell wall proteins and 19 cytosol proteins were identified and mapped, with 9 and 10, respectively, being novel proteins. One of the novel proteins was not predicted in the genome project, and for four of the identified proteins alternative start codons were suggested. Fourteen of the culture filtrate proteins were proposed to possess signal sequences. Seven of these proteins were microsequenced and the N-terminal sequences obtained confirmed the prediction. The data presented here are an important complement to the genetic information, and the established 2-D PAGE maps (also available at: [www.ssi.dk/publichealth/tbimmun](http://www.ssi.dk/publichealth/tbimmun)) provide a basis for comparative studies of protein expression.

L14 ANSWER 25 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 20

AN 2000:124885 BIOSIS

DN PREV200000124885

TI High resolution electroelution of polyacrylamide gels for the purification of single proteins from *Mycobacterium tuberculosis* culture filtrate.

AU Weldingh, K.; Hansen, A.; Jacobsen, S.; Andersen, P. [Reprint author]

CS Department of TB-Immunology, Statens Serum Institut, Artillerivej 5, DK-2300, Copenhagen S, Denmark

SO Scandinavian Journal of Immunology, (Jan., 2000) Vol. 51, No. 1, pp. 79-86. print.  
CODEN: SJIMAX. ISSN: 0300-9475.

DT Article

LA English

ED Entered STN: 5 Apr 2000  
Last Updated on STN: 3 Jan 2002

AB Culture filtrate from *Mycobacterium tuberculosis* contains protective molecules which have been used successfully in experimental vaccines against tuberculosis. Despite an increasing number of mycobacterial proteins being characterised, a major effort is still needed to get an overview of the many potentially interesting molecules in culture filtrate. In this study we describe a high throughput method for purification and biological evaluation of protein components in complex protein mixtures. The method presents a new application of the recently developed Mini Whole Gel Eluter and employs this apparatus for the high resolution electroelution of selected molecular mass fractions of protein mixtures previously separated in large polyacrylamide gels. Two novel *M. tuberculosis* culture filtrate proteins (CspA and TB18.6) were purified by this method, their N-terminal sequences were determined and the open reading frame encoding each of the proteins identified. The immunological recognition of the molecules were evaluated in tuberculosis infected mice and guinea pigs. Both proteins induced DTH responses in guinea pigs and IFN-gamma release from spleen lymphocytes isolated from infected mice.

L14 ANSWER 26 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 21

AN 2000:34114 BIOSIS

DN PREV20000034114

TI Differential T-cell recognition of native and recombinant *Mycobacterium tuberculosis* GroES.

AU Rosenkrands, Ida; Weldingh, Karin; Ravn, Pernille; Brandt, Lise; Hojrup, Peter; Rasmussen, Peter Birk; Coates, Anthony R.; Singh, Mahavir; Mascagni, Paolo; Andersen, Peter [Reprint author]

CS Department of TB Immunology, Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen S, Denmark

SO Infection and Immunity, (Nov., 1999) Vol. 67, No. 11, pp. 5552-5558.  
print.  
CODEN: INFIBR. ISSN: 0019-9567.

DT Article  
LA English  
ED Entered STN: 19 Jan 2000  
Last Updated on STN: 31 Dec 2001

AB **Mycobacterium tuberculosis** GroES was purified from culture filtrate, and its identity was confirmed by immunoblot analysis and N-terminal sequencing. Comparing the immunological recognition of native and recombinant GroES, we found that whereas native GroES elicited a strong proliferative response and release of gamma interferon-gamma by peripheral blood mononuclear cells from healthy tuberculin reactors, the recombinant protein failed to do so. The same difference in immunological recognition was observed in a mouse model of TB infection. Both the native and recombinant preparations were recognized by mice immunized with the recombinant protein. Biochemical characterization including sodium dodecyl sulfate-polyacrylamide gel electrophoresis, two-dimensional electrophoresis, and mass spectrometry analysis of both proteins demonstrated no differences between the native and recombinant forms of GroES except for the eight additional N-terminal amino acids derived from the fusion partner inrecombinant GroES. The recombinant fusion protein, still tagged with the maltose binding protein, was recognized by T cells isolated from TB-infected mice if mixed with culture filtrate before affinity purification on an amylose column. The maltose binding protein treated in the same manner as a control preparation was not recognized. Based on the data presented, we suggest that the association of biologically active molecules from culture filtrate with the chaperone GroES may be responsible for the observed T-cell recognition of the native preparation.

L14 ANSWER 27 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 22

AN 1999:146249 BIOSIS  
DN PREV199900146249  
TI Immunological evaluation of novel **Mycobacterium tuberculosis** culture filtrate proteins.  
AU Weldingh, Karin; Andersen, Peter [Reprint author]  
CS Dep. TB Immunol., Statens Serum Inst., Artillerivej 5, DK-2300 Copenhagen S, Denmark  
SO FEMS Immunology and Medical Microbiology, (Feb., 1999) Vol. 23, No. 2, pp. 159-164. print.  
ISSN: 0928-8244.

DT Article  
LA English  
ED Entered STN: 13 Apr 1999  
Last Updated on STN: 13 Apr 1999

AB Culture filtrate from **Mycobacterium tuberculosis** contains molecules which can promote protective immunity to tuberculosis in animal models. Six novel proteins in the region of 17-29 kDa were purified and investigated for their immunological relevance in *M. tuberculosis*-infected mice, guinea pigs and tuberculosis patients. The proteins CFP17, CFP21, CFP25 and CFP29 were all identified as strong interferon-gamma inducers in *M. tuberculosis*-infected mice and in tuberculosis patients. The CFP21 protein is encoded in the genomic region RD-2 which is deleted from a number of BCG strains and the diagnostic potential of this antigen was evaluated.

L14 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2006 ACS on STN  
AN 1998:684968 CAPLUS  
DN 129:300060  
TI Novel antigens of **Mycobacterium tuberculosis** culture filtrates and the genes encoding and their diagnostic and prophylactic use  
IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin ; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter  
PA Statens Serum Institut, Den.  
SO PCT Int. Appl., 264 pp.  
CODEN: PIXXD2  
DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	AA	19981008	CA 1998-2285625	19980401
	AU 9868204	A1	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 20011515359	T2	20010918	JP 1998-541074	19980401
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	CA 2319380	AA	19990520	CA 1998-2319380	19981008
	WO 9924577	A1	19990520	WO 1998-DK438	19981008
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1029053	A1	20000823	EP 1998-947412	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	NZ 504951	A	20010629	NZ 1998-504951	19981008
	AU 750173	B2	20020711	AU 1998-94338	19981008
	EP 1484405	A1	20041208	EP 2004-77071	19981008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	EP 1998-913536	A3	19980401		
	WO 1998-DK132	W	19980401		
	EP 1998-947412	A3	19981008		
	WO 1998-DK438	W	19981008		

AB Culture filtrate antigens of *Mycobacterium tuberculosis* are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 29 OF 29 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 23

AN 1998:393332 BIOSIS

DN PREV199800393332

TI Two-dimensional electrophoresis for analysis of *Mycobacterium* tuberculosis culture filtrate and purification and characterization of six

AU novel proteins.  
AU Weldingh, Karin; Rosenkrands, Ida; Jacobsen, Susanne; Rasmussen,  
AU Peter Birk; Elhay, Martin J.; Andersen, Peter [Reprint author]  
CS Dep. TB Immunol., Statens Serum Inst., Artillerivej 5, DK-2300 Copenhagen,  
Denmark  
SO Infection and Immunity, (Aug., 1998) Vol. 66, No. 8, pp. 3492-3500. print.  
CODEN: INFIBR. ISSN: 0019-9567.  
DT Article  
LA English  
ED Entered STN: 10 Sep 1998  
Last Updated on STN: 10 Sep 1998  
AB Culture filtrate from *Mycobacterium tuberculosis* contains molecules which promote high levels of protective immunity in animal models of subunit vaccination against tuberculosis. We have used two-dimensional electrophoresis for analysis and purification of six novel *M. tuberculosis* culture filtrate proteins (CFPs): CFP17, CFP20, CFP21, CFP22, CFP25, and CFP28. The proteins were tested for recognition by *M. tuberculosis*-reactive memory cells from different strains of inbred mice and for their capacity to induce a skin test response in *M. tuberculosis*-infected guinea pigs. CFP17, CFP20, CFP21 and CFP25 induced both a high gamma interferon release and a strong delayed-type hypersensitivity response, and CFP21 was broadly recognized by different strains of inbred mice. N-terminal sequences were obtained for the six proteins, and the corresponding genes were identified in the Sanger *M. tuberculosis* genome database. In parallel we established a two-dimensional electrophoresis reference map of short-term culture filtrate components and mapped novel proteins as well as already-known CFP.

=> e florio walter/au  
E1 7 FLORIO VITO V/AU  
E2 75 FLORIO W/AU  
E3 38 --> FLORIO WALTER/AU  
E4 1 FLORIOA TULLIO/AU  
E5 5 FLORIOLI A/AU  
E6 1 FLORIOLI A C/AU  
E7 1 FLORIOLI G/AU  
E8 3 FLORIOLLI R Y/AU  
E9 2 FLORIOLLI RENEE Y/AU  
E10 14 FLORION A/AU  
E11 6 FLORION ANDRE/AU  
E12 1 FLORIOS N S/AU

=> s e2-e3 and mycobact?  
L15 90 ("FLORIO W"/AU OR "FLORIO WALTER"/AU) AND MYCOBACT?

=> dup rem l15  
PROCESSING COMPLETED FOR L15  
L16 20 DUP REM L15 (70 DUPLICATES REMOVED)

=> d bib ab 1-  
YOU HAVE REQUESTED DATA FROM 20 ANSWERS - CONTINUE? Y/ (N) :y

L16 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1  
AN 2006:135438 CAPLUS  
TI Influence of culture medium on the resistance and response of *Mycobacterium bovis* BCG to reactive nitrogen intermediates  
AU Florio, Walter; Batoni, Giovanna; Esin, Semih; Bottai, Daria;  
Maisetta, Giuseppantonio; Favilli, Flavia; Brancatisano, Franca L.; Campa,  
Mario  
CS Dipartimento di Patologia Sperimentale, Biotecnologie Mediche,  
Infettivologia ed Epidemiologia, Universita di Pisa, Pisa, 56127, Italy  
SO Microbes and Infection (2006), 8(2), 434-441  
CODEN: MCINFS; ISSN: 1286-4579  
PB Elsevier B.V.  
DT Journal  
LA English

AB The aim of the present work was to evaluate the influence of the culture medium on the resistance and response of *Mycobacterium bovis* BCG to reactive nitrogen intermediates, *in vitro*. BCG was grown in Sauton, Dubos or Middlebrook 7H9 medium and exposed to sodium nitroprusside (SNP) for up to 7 days. The percentage of bacilli that survived was significantly lower in Middlebrook 7H9 than in Sauton or Dubos medium. Addition of SNP to Middlebrook 7H9 caused an increase in the RedOx potential in either the absence or the presence of BCG, while addition of the compound to Sauton medium gave rise to an increase in the RedOx potential only in the absence of bacteria, whereas a decrease in the RedOx potential was observed in the presence of BCG. The resistance of BCG to SNP in the different media did not correlate with the concentration of peroxynitrite in culture supernatants. BCG grown in different media showed a differential protein expression pattern, as assessed by two-dimensional gel electrophoresis. Exposure of BCG to sub-lethal concns. of SNP in Middlebrook 7H9, but not in Sauton medium, revealed a differential expression of at least 38 protein species. Altogether these results demonstrate that the growth medium may have a remarkable influence on the resistance and the response of BCG to SNP and suggest that the different resistance of BCG in the two media is unlikely to be due to a differential antioxidant effect of the medium itself.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 2  
AN 2006:143057 BIOSIS  
DN PREV200600146194  
TI Human CD56(bright) CD56(dim) natural killer cell subsets respond differentially to direct stimulation with *Mycobacterium bovis* bacillus Calmette-Guerin.  
AU Batoni, G. [Reprint Author]; Esin, S.; Favilli, F.; Pardini, M.; Bottai, D.; Maisetta, G.; Florio, W.; Campa, M.  
CS Univ Pisa, Dipartimento Patol Sperimentale Biotecnol Med Inf, Via San Zeno 35-39, I-56127 Pisa, Italy  
batoni@biomed.unipi.it  
SO Scandinavian Journal of Immunology, (DEC 2005) Vol. 62, No. 6, pp. 498-506.  
CODEN: SJIMAX. ISSN: 0300-9475.  
DT Article  
LA English  
ED Entered STN: 22 Feb 2006  
Last Updated on STN: 22 Feb 2006  
AB *Mycobacterium bovis* bacillus Calmette-Guerin (BCG) is capable of directly stimulating several effector functions of human natural killer (NK) cells in the absence of interleukin-12 and professional antigen presenting cells. To assess the contribution of two main human NK-cell subsets (CD56(dim) and CD56(bright)) to the overall *in vitro* NK-cell response to BCG, peripheral blood mononuclear cells depleted of nylon wool-adherent cells or purified NK cells were stimulated with live BCG. By combining intranuclear bromodeoxyuridine (BrdU) staining and analysis of CD56 marker intensity, statistically higher percentages of BrdU<sup>+</sup> cells were found among the CD56(bright) subset than the CD56(dim) subset after 6 days of stimulation with BCG. Similarly, evaluation of intracellular interferon-gamma (IFN-gamma) revealed that CD56(bright) cells were those mainly involved in IFN-gamma production in response to BCG. In contrast, the CD56(dim) subset contained higher levels of perforin and granzyme A, two key molecules for exocytosis-mediated cytotoxicity, than the CD56(bright) subset. Although 16-20-h stimulation with BCG did not substantially alter the expression of cytotoxic molecules(dim), by the two subsets, a decrease in perforin content was observed in the CD56, but not in the CD56(bright) subset, following 4-h incubation with the NK-sensitive target K562 cell line. This decrease in perforin content correlated with the induction by BCG-stimulated NK cells, of early markers of apoptosis on target cells to a greater extent than unstimulated cells suggesting a major role for the CD56(dim) subset in cytotoxic activity in response to BCG. Taken together, these results demonstrate that CD56(bright) and CD56(dim) human NK-cell subsets exert different functional activities in response to a live bacterial pathogen.

L16 ANSWER 3 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 3

AN 2005:271995 BIOSIS  
DN PREV200510062059

TI Disruption of the gene encoding for secretion antigen SA5K affects growth of *Mycobacterium bovis* bacillus Calmette-Guerin in human macrophages and in mice.

AU Bottai, Daria; Esin, Semih; Batoni, Giovanna [Reprint Author]; Pardini, Manuela; Maisetta, Giuseppantonio; Donati, Valentina; Favilli, Flavia; Florio, Walter; Campa, Mario

CS Univ Pisa, Dipartimento Patol Sperimentale Biotecnol Med Inf, Pisa, Italy  
batoni@biomed.unipi.it

SO Research in Microbiology, (APR 2005) Vol. 156, No. 3, pp. 393-402.  
CODEN: RMCREW. ISSN: 0923-2508.

DT Article  
LA English  
ED Entered STN: 21 Jul 2005  
Last Updated on STN: 21 Jul 2005

AB An 8.3-kDa secretory antigen of *Mycobacterium bovis* bacillus Calmette-Guerin (BCG), called SA5K, was previously identified and characterized in our laboratory. Sequence analysis of the BCG sa5k gene, including the corresponding promoter region, showed that it is identical to the homologous gene in *Mycobacterium tuberculosis* (Rv1174c). No significant homology with other proteins was found and the physiologic role of SA5K for mycobacteria remains unknown. In the present study, a BCG mutant strain (BCGsa5k::aph) was constructed by allelic exchange involving the replacement of the sa5k gene with a kanamycin-inactivated copy. Mutant and parental strains showed similar growth rates in liquid medium, suggesting that the loss of the sa5k gene does not affect the in vitro growth of BCG. Nevertheless, BCGsa5k::aph showed a reduced ability to grow in human macrophages compared with the wild-type BCG, suggesting that SA5K is involved in intracellular survival/multiplication mechanisms. The mutant strain was also attenuated in vivo in a mouse infection model, showing impaired growth/survival in spleen and liver and fewer and smaller granulomatous lesions compared to the parental strain. Complementation of the mutation restored the parental phenotype. Taken together, results presented in this study suggest a role for SA5K in the growth capacity of BCG both in an intracellular milieu and in infected mice. (c) 2004 Elsevier SAS. All rights reserved.

L16 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4

AN 2004:490265 CAPLUS  
DN 141:52841

TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to *M. tuberculosis*, and use thereof as vaccines and in diagnosis

IN Andersen, Peter; Skiot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter  
PA Den.  
SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.  
CODEN: USXXCO

DT Patent  
LA English  
FAN.CNT 10

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
PI US 20041115211	A1	20040617	US 2003-620246	20030715
US 6641814	B1	20031104	US 1998-50739	19980330
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI DK 1997-376	A	19970402		
US 1997-44624P	P	19970418		
DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
US 1998-50739	A2	19980330		

DK 1998-1281 A 19981008  
EP 1998-913536 A3 19980401

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

L16 ANSWER 5 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 5

AN 2004:300252 BIOSIS

DN PREV200400301569

TI Functional characterization of human natural killer cells responding to *Mycobacterium bovis* bacille Calmette-Guerin.

AU Esin, Semih [Reprint Author]; Batoni, Giovanna; Pardini, Manuela; Favilli, Flavia; Bottai, Daria; Maisetta, Giuseppantonio; Florio, Walter; Vanacore, Renayo; Wigzell, Hans; Campa, Mario

CS Dipartimento Patol Sperimentale Biotecnol Med Inf, Univ Pisa, Via S Zeno 35-39, I-56127, Pisa, Italy  
esin@biomed.unipi.it

SO Immunology, (May 2004) Vol. 112, No. 1, pp. 143-152. print.  
CODEN: IMMUAM. ISSN: 0019-2805.

DT Article

LA English

ED Entered STN: 30 Jun 2004

Last Updated on STN: 30 Jun 2004

AB The kinetics of activation and induction of several effector functions of human natural killer (NK) cells in response to *Mycobacterium bovis* bacille Calmette-Guerin (BCG) were investigated. Owing to the central role of monocytes/macrophages (MM) in the initiation and maintenance of the immune response to pathogens, two different experimental culture conditions were analysed. In the first, monocyte-depleted nylon wool non-adherent (NW) cells from healthy donors were stimulated with autologous MM preinfected with BCG (intracellular BCG). In the second, the NW cells were directly incubated with BCG, which was therefore extracellular. In the presence of MM, CD4+ T lymphocytes were the cell subset mainly expressing the activation marker, CD25, and proliferating with a peak after 7 days of culture. In contrast, in response to extracellular BCG, the peak of the proliferative response was observed after 6 days of stimulation, and CD56+ CD3- cells (NK cells) were the cell subset preferentially involved. Such proliferation of NK cells did not require a prior sensitization to mycobacterial antigens, and appeared to be dependent upon contact between cell populations and bacteria. Following stimulation with extracellular BCG, the majority of interferon-gamma (IFN-gamma)-producing cells were NK cells, with a peak IFN-gamma production at 24-30 hr. Interleukin (IL)-2 and IL-4 were not detectable in NK cells or in CD3+ T lymphocytes at any time tested. IL-12 was not detectable in the culture supernatant of NW cells stimulated with extracellular BCG. Compared to the non-stimulated NW cells, the NW cells incubated for 16-20 hr with BCG induced the highest levels of expression of apoptotic/death marker on the NK-sensitive K562 cell line. BCG also induced expression of the activation marker, CD25, and proliferation, IFN-gamma production and cytotoxic activity, on negatively selected CD56+ CD3- cells. Altogether, the results of this study demonstrate that extracellular mycobacteria activate several NK-cell functions and suggest a possible alternative mechanism of NK-cell activation as the first line of defence against mycobacterial infections.

L16 ANSWER 6 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 6

AN 2004:5335 BIOSIS

DN PREV200400007544

TI Nucleic acids fragments and polypeptide fragments derived from *M. tuberculosis*.

AU Andersen, Peter [Inventor, Reprint Author]; Nielsen, Rikke [Inventor]; Oettinger, Thomas [Inventor]; Rasmussen, Peter Birk [Inventor]; Rosenkrands, Ida [Inventor]; Weldingh, Karin [Inventor]; **Florio, Walter** [Inventor]  
 CS Bronshoj, Denmark  
 ASSIGNEE: Statens Serum Institut, Copenhagen, Denmark  
 PI US 6641814 20031104  
 SO Official Gazette of the United States Patent and Trademark Office Patents, (Nov 4 2003) Vol. 1276, No. 1. <http://www.uspto.gov/web/menu/patdata.html>. e-file.  
 ISSN: 0098-1133 (ISSN print).  
 DT Patent  
 LA English  
 ED Entered STN: 17 Dec 2003  
 Last Updated on STN: 17 Dec 2003  
 AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.  
 L16 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7  
 AN 2003:696302 CAPLUS  
 DN 139:229237  
 TI Protein and DNA sequences of antigens from *Mycobacterium* and uses in tuberculosis diagnosis and treatment  
 IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; **Florio, Walter**; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk  
 PA Statens Serum Institut, Den.  
 SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428. CODEN: USXXCO  
 DT Patent  
 LA English  
 FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6982085	B2	20060103		
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
	US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	US 2001-791171	B2	20010220		
	US 2002-60428	A2	20020129		
	EP 1998-913536	A3	19980401		
AB	The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from <i>Mycobacterium tuberculosis</i> . The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing tuberculosis caused by virulent mycobacteria, e.g. by <i>Mycobacterium tuberculosis</i> , <i>Mycobacterium africanum</i> or <i>Mycobacterium</i>				

bovis, in an animal, including a human being. The invention related to treating tuberculosis using antigens isolated from **Mycobacterium** tuberculosis.

L16 ANSWER 8 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 8  
AN 2003:330001 BIOSIS  
DN PREV200300330001  
TI Identification of novel proteins in culture filtrates of **Mycobacterium bovis** bacillus Calmette-Guerin in the isoelectric point range 6-11.  
AU **Florio, Walter** [Reprint Author]; Batoni, Giovanna; Esin, Semih;  
Bottai, Daria; Maisetta, Giuseppantonio; Pardini, Manuela; Campa, Mario  
CS Dipartimento di Patologia Sperimentale, Biotecnologie Mediche,  
Infettivologia ed Epidemiologia, Universita di Pisa, Via S. Zeno 35-39,  
I-56127, Pisa, Italy  
florio@biomed.unipi.it  
SO Proteomics, (May 2003) Vol. 3, No. 5, pp. 798-802. print.  
ISSN: 1615-9853 (ISSN print).  
DT Article  
LA English  
ED Entered STN: 16 Jul 2003  
Last Updated on STN: 16 Jul 2003  
AB Two-dimensional gel electrophoresis and mass spectrometry were used to identify proteins in the isoelectric point range 6-11 in culture filtrates of **Mycobacterium bovis** bacillus Calmette-Guerin (BCG). Twelve proteins were identified, three of which had not been described previously. The expression of the identified proteins was comparatively analyzed in culture filtrates of BCG in different growth phases and culture conditions. For some of these proteins, the relative protein abundance in the different culture filtrate preparations was significantly different. The differential expression of the identified proteins is discussed in relation to their putative localization and/or biological function.

L16 ANSWER 9 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 9  
AN 2003:575450 BIOSIS  
DN PREV200300580948  
TI Expression of SA5K, a secretion antigen of **Mycobacterium** tuberculosis, inside human macrophages and in sputum from tuberculosis patients.  
AU Bottai, Daria; Batoni, Giovanna [Reprint Author]; Esin, Semih; Maisetta, Giuseppantonio; Pardini, Manuela; **Florio, Walter**; Rindi, Laura;  
Garzelli, Carlo; Campa, Mario  
CS Dipartimento di Patologia Sperimentale, Biotecnologie Mediche,  
Infettivologia ed Epidemiologia, Universita degli Studi di Pisa, Via S. Zeno 35-39, 56127, Pisa, Italy  
batoni@biomed.unipi.it  
SO FEMS Microbiology Letters, (26 September 2003) Vol. 226, No. 2, pp. 229-235. print.  
CODEN: FMLED7. ISSN: 0378-1097.  
DT Article  
LA English  
ED Entered STN: 10 Dec 2003  
Last Updated on STN: 10 Dec 2003  
AB An 8.3 kDa protein (SA5K), secreted by **Mycobacterium** tuberculosis/**Mycobacterium bovis** bacillus Calmette-Guerin (BCG) in culture filtrate, has been previously described in our laboratory. In the present study, analysis of the distribution of SA5K gene (Rv1174c) among M. tuberculosis strains, isolated from a wide variety of clinical specimens, revealed that the gene is present in all clinical isolates analyzed (29/29). SA5K expression inside human macrophages infected with BCG was demonstrated by reverse transcription-polymerase chain reaction (RT-PCR) on RNA extracted from bacterial cells following 24 and 48 h of infection. In addition, in order to evaluate whether SA5K gene was also expressed at the site of infection in the lung, a nested RT-PCR assay was developed to detect specific mRNA in sputum samples collected from smear positive tuberculosis patients. SA5K mRNA was detected in all the samples

containing high numbers of tubercle bacilli demonstrating that the corresponding gene is expressed during the course of clinical infection.

L16 ANSWER 10 OF 20 USPATFULL on STN  
AN 2002:178550 USPATFULL  
TI Nucleic acid fragments and polypeptide fragments derived from M. tuberculosis  
IN Andersen, Peter, Bronshoj, DENMARK  
Nielsen, Rikke, Frederiksberg C, DENMARK  
Oettinger, Thomas, Hellerup, DENMARK  
Rasmussen, Peter Birk, Kobenhaven O, DENMARK  
Rosenkrands, Ida, Kobenhaven O, DENMARK  
Weldingh, Karin, Kobenhaven N, DENMARK  
Florio, Walter, Frederiksberg C, DENMARK  
PA STATENS SERUM INSTITUT (non-U.S. corporation)  
PI US 2002094336 A1 20020718  
AI US 2001-791171 A1 20010220 (9)  
RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING  
PRAI DK 1997-376 19970402  
DK 1997-1277 19971110  
US 1997-44624P 19970418 (60)  
US 1998-70488P 19980105 (60)  
DT Utility  
FS APPLICATION  
LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151  
CLMN Number of Claims: 53  
ECL Exemplary Claim: 1  
DRWN 6 Drawing Page(s)  
LN.CNT 6134

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is based on the identification and characterization of a number of M. tuberculosis derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L16 ANSWER 11 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 10  
AN 2002:448834 BIOSIS  
DN PREV200200448834  
TI Identification, molecular cloning, and evaluation of potential use of isocitrate dehydrogenase II of *Mycobacterium bovis* BCG in serodiagnosis of tuberculosis.  
AU Florio, W. [Reprint author]; Bottai, D.; Batoni, G.; Esin, S.; Pardini, M.; Maisetta, G.; Campa, M.  
CS Dipartimento di Patologia Sperimentale, Biotecnologie Mediche, Infettivologia ed Epidemiologia, Universita di Pisa, Via S. Zeno 35-39, 56127, Pisa, Italy  
florio@biomed.unipi.it  
SO Clinical and Diagnostic Laboratory Immunology, (July, 2002) Vol. 9, No. 4, pp. 846-851. print.  
ISSN: 1071-412X.  
DT Article  
LA English  
ED Entered STN: 21 Aug 2002  
Last Updated on STN: 21 Aug 2002  
AB Diagnosis of tuberculosis is time-consuming and requires infrastructures which are often not available in countries with high incidences of the disease. In the present study, an 82-kDa protein antigen was isolated by affinity chromatography and was identified by peptide mass fingerprinting as isocitrate dehydrogenase II, which is encoded by the icd2 gene of *Mycobacterium bovis* BCG. The icd2 gene of BCG was cloned by PCR, and the product of recombinant gene expression was purified and analyzed

by two-dimensional polyacrylamide gel electrophoresis. The recombinant protein, named rICD2, was tested for its recognition by immunoglobulin G (IgG) antibodies from the sera of 16 patients with tuberculosis (TB) and 23 healthy individuals by Western blotting. The results showed that rICD2 is recognized by IgG antibodies from the sera of all TB patients tested at serum dilutions of  $\geq 1:640$ . At a serum dilution of 1:1,280, the sensitivity was 50% and the specificity was 86.9%. These results indicate that rICD2 might represent a candidate for use in a new assay for the serodiagnosis of TB.

L16 ANSWER 12 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 11

AN 2002:440112 BIOSIS

DN PREV200200440112

TI Purification, biochemical characterization and immunogenicity of SA5K, a secretion antigen of **Mycobacterium tuberculosis**.

AU Batoni, G. [Reprint author]; Bottai, D.; Esin, S.; **Florio, W.**; Pardini, M.; Maisetta, G.; Freer, G.; Senesi, S.; Campa, M.

CS Dipartimento di Patologia Sperimentale, Biotecnologie Mediche, Infettivologia ed Epidemiologia, University of Pisa, Via S. Zeno 35-39, 56127, Pisa, Italy  
batoni@biomed.unipi.it

SO Scandinavian Journal of Immunology, (July, 2002) Vol. 56, No. 1, pp. 43-51. print.  
CODEN: SJIMAX. ISSN: 0300-9475.

DT Article

LA English

ED Entered STN: 14 Aug 2002  
Last Updated on STN: 14 Aug 2002

AB **Mycobacterium tuberculosis** (MTB) secretory proteins are generally considered important antigens for immune protection against tuberculosis (TB). An 8.3-kDa secretory antigen of MTB and **Mycobacterium bovis** bacillus Calmette-Guerin (BCG), called SA5K, was recently identified and cloned in our laboratory. In this report, recombinant SA5K containing a histidine hexamer was expressed in *Escherichia coli* and purified to investigate its biochemical structure and to establish whether it was immunogenic for healthy sensitized and nonsensitized human donors and for patients infected with MTB. The protein nucleotide sequence was shown to be identical in BCG and in MTB. SA5K revealed an abnormal electrophoretic mobility in SDS-PAGE that made it look lighter than it is in Western blotting. While recombinant SA5K was poorly recognized by T lymphocytes from patients with pulmonary TB, it elicited proliferation of CD4+ T lymphocytes in the vast majority of healthy individuals sensitized to mycobacterial antigens by BCG vaccination. At a serum dilution of 1: 80, antibodies reacting against recombinant SA5K were found in 67% of sera from TB patients and in 73% of sera from healthy subjects. The percentage of positive subjects dropped at higher serum dilutions, but no significant difference in the recognition rate was observed between TB patients and healthy donors and between healthy vaccinated and nonvaccinated subjects. Owing to the high percentage of sera from healthy subjects who recognized SA5K in Western blotting, the antigen seems to exhibit, at least in the present form, a poor specificity for an employment for a serodiagnosis of TB.

L16 ANSWER 13 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 12

AN 2002:73581 BIOSIS

DN PREV200200073581

TI Involvement of the **Mycobacterium tuberculosis** secreted antigen SA-5K in intracellular survival of recombinant **Mycobacterium smegmatis**.

AU Batoni, Giovanna [Reprint author]; Bottai, Daria; Maisetta, Giuseppantonio; Pardini, Manuela; Boschi, Antonella; **Florio, Walter**; Esin, Semih; Campa, Mario

CS Dipartimento di Patologia Sperimentale, Biotecnologie Mediche, Infettivologia ed Epidemiologia, University of Pisa, Via S. Zeno 35-39, Pisa, Italy  
batoni@biomed.unipi.it

SO FEMS Microbiology Letters, (27 November, 2001) Vol. 205, No. 1, pp.

125-129. print.

CODEN: FMLED7. ISSN: 0378-1097.

DT Article

LA English

ED Entered STN: 16 Jan 2002

Last Updated on STN: 25 Feb 2002

AB A new protein (SA-5K) secreted in culture filtrates by *Mycobacterium bovis*, *Mycobacterium tuberculosis*, and few other mycobacterial species was previously identified and purified in our laboratory. In order to evaluate the putative role of SA-5K during intracellular mycobacterial growth, in the present study the SA-5K gene was cloned and expressed in *Mycobacterium smegmatis*, a rapid growing non-pathogenic mycobacterium which does not contain the gene for the protein. SA-5K expression in the THP-1 human macrophage cell line infected with the recombinant strain, (M. *smegmatis*-pROL5K) was demonstrated by RT-PCR on RNA extracted from bacterial cells following 24 and 48 h of infection. Intracellular SA5K expression was associated with a higher cfu increase of M. *smegmatis*-pROL5K in comparison to the negative control strain (M. *smegmatis* recombinant for the cloning vector) (P=0.01). No significant change in SA-5K synthesis by M. *smegmatis*-pROL5K was observed when the recombinant strain was grown in vitro in different stress conditions such as iron deprivation, pH 4.5, presence of nitric oxide or hydrogen peroxide. The results presented in this study suggest a possible role for SA-5K in intracellular survival of recombinant M. *smegmatis*, though the function of the protein remains unknown.

L16 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2000:260319 CAPLUS

DN 132:292711

TI Tb vaccine and diagnostic based on antigens from the *Mycobacterium tuberculosis* cell

IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Veggerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rosenkrands, Ida

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 126 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000021983	A2	20000420	WO 1999-DK538	19991008
	WO 2000021983	A3	20001123		
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2346218	AA	20000420	CA 1999-2346218	19991008
	AU 9960784	A1	20000501	AU 1999-60784	19991008
	AU 766093	B2	20031009		
	EP 1117683	A2	20010725	EP 1999-947257	19991008
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, IE, SI, LT, LV, FI, RO				

PRAI DK 1998-1281 A 19981008  
US 1999-116673P P 19990121  
WO 1999-DK538 W 19991008

AB The present invention relates to substantially pure polypeptides, which has a sequence identity of at least 80 % to an amino acid sequence disclosed, or which is a subsequence of at least 6 amino acids thereof, preferably a B- or T-cell epitope of the polypeptides disclosed. The polypeptide or the subsequence thereof has at least one of nine properties. The use of the disclosed polypeptides in medicine is disclosed, preferably as vaccine or diagnostic agents relating to virulent

**Mycobacterium.** The invention further relates to the nucleotide sequences disclosed and the nucleotide sequences encoding the disclosed polypeptides. Medical and non-medical use of the nucleotide sequences is disclosed.

L16 ANSWER 15 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN  
DUPLICATE 13

AN 2000:271567 BIOSIS

DN PREV200000271567

TI Mapping and identification of **Mycobacterium tuberculosis** proteins by two-dimensional gel electrophoresis, microsequencing and immunodetection.

AU Rosenkrands, Ida; Weldingh, Karin; Jacobsen, Susanne; Hansen, Christina Vegerby; **Florio, Walter**; Gianetri, Isabella; Andersen, Peter [Reprint author]

CS Department of TB Immunology, Statens Serum Institute, 5 Artillerivej, DK-2300, Copenhagen S, Denmark

SO Electrophoresis, (March, 2000) Vol. 21, No. 5, pp. 935-948. print.  
CODEN: ELCTDN. ISSN: 0173-0835.

DT Article

LA English

ED Entered STN: 30 Jun 2000

Last Updated on STN: 5 Jan 2002

AB **Mycobacterium tuberculosis** is the infectious agent giving rise to human tuberculosis. The entire genome of *M. tuberculosis*, comprising approximately 4000 open reading frames, has been sequenced. The huge amount of information released from this project has facilitated proteome analysis of *M. tuberculosis*. Two-dimensional polyacrylamide gel electrophoresis (2-D PAGE) was applied to fractions derived from *M. tuberculosis* culture filtrate, cell wall, and cytosol, resulting in the resolution of 376, 413, and 395 spots, respectively, in silver-stained gels. By microsequencing and immunodetection, 38 culture filtrate proteins were identified and mapped, of which 12 were identified for the first time. In the same manner, 23 cell wall proteins and 19 cytosol proteins were identified and mapped, with 9 and 10, respectively, being novel proteins. One of the novel proteins was not predicted in the genome project, and for four of the identified proteins alternative start codons were suggested. Fourteen of the culture filtrate proteins were proposed to possess signal sequences. Seven of these proteins were microsequenced and the N-terminal sequences obtained confirmed the prediction. The data presented here are an important complement to the genetic information, and the established 2-D PAGE maps (also available at: [www.ssi.dk/publichealth/tbimmun](http://www.ssi.dk/publichealth/tbimmun)) provide a basis for comparative studies of protein expression.

L16 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1998:684968 CAPLUS

DN 129:300060

TI Novel antigens of **Mycobacterium tuberculosis** culture filtrates and the genes encoding and their diagnostic and prophylactic use

IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; **Florio, Walter**

PA Statens Serum Institut, Den.

SO PCT Int. Appl., 264 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			

CA 2285625	AA	19981008	CA 1998-2285625	19980401
AU 9868204	A1	19981022	AU 1998-68204	19980401
AU 740545	B2	20011108		
EP 972045	A1	20000119	EP 1998-913536	19980401
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001515359	T2	20010918	JP 1998-541074	19980401
EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
CA 2319380	AA	19990520	CA 1998-2319380	19981008
WO 9924577	A1	19990520	WO 1998-DK438	19981008
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1029053	A1	20000823	EP 1998-947412	19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
NZ 504951	A	20010629	NZ 1998-504951	19981008
AU 750173	B2	20020711	AU 1998-94338	19981008
EP 1484405	A1	20041208	EP 2004-77071	19981008
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI DK 1997-376	A	19970402		
US 1997-44624P	P	19970418		
DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
EP 1998-913536	A3	19980401		
WO 1998-DK132	W	19980401		
EP 1998-947412	A3	19981008		
WO 1998-DK438	W	19981008		

AB Culture filtrate antigens of *Mycobacterium tuberculosis* are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 17 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 14

AN 1998:318486 BIOSIS

DN PREV199800318486

TI Identification and molecular cloning of a novel secretion antigen from *Mycobacterium tuberculosis* and *Mycobacterium bovis* BCG.

AU Freer, G. [Reprint author]; Florio, W.; Dalla Casa, B.; Bottai, D.; Batoni, G.; Maisetta, G.; Senesi, S.; Campa, M.

CS Dip. Patol. Sper., Bioteecnol. Med. Infettivol. Epidemiol., Univ. Studi Pisa, Via S. Zeno 35-39, 56127 Pisa, Italy

SO Research in Microbiology, (April, 1998) Vol. 149, No. 4, pp. 265-275.  
print.

CODEN: RMCREW. ISSN: 0923-2508.

DT Article

LA English

OS Genbank-AD000020

ED Entered STN: 22 Jul 1998

Last Updated on STN: 22 Jul 1998

AB A novel protein called SA-5K was identified in *Mycobacterium*

bovis BCG (BCG) short-term culture filtrates (CFs) by means of a recently described monoclonal antibody (mAb), L8D8. This protein had an apparent molecular mass (MM) of 5 kDa, as judged by Western blotting after sodium dodecyl sulphate-polyacrylamide gel electrophoresis in reducing conditions, and did not seem to contain any sugar or lipid substituents. In the present work, SA-SK was purified from BCG CFs by affinity chromatography. A protein that could be detected in Western blot but not by standard protein staining techniques was obtained. When SA-5K was subjected to aminoterminal sequencing, the 10 amino acids (aa) found matched the first 10-aa sequence deduced from an open reading frame (ORF) of *M. tuberculosis*. The ORF encodes a polypeptide, likely to include a signal for secretion, with an estimated MM of 8.3 kDa after signal peptide cleavage. The secretory nature of SA-5K was confirmed by the fact that it could only be detected in CFs, but not in other BCG subcellular fractions. After size exclusion chromatography, reactivity with mAb L8D8 was found to peak in the 45-50- and 14-16-kDa fractions. The latter MM was close to that estimated from the ORF of *M. tuberculosis*; implying that the 5-kDa antigen detected initially by Western blot in reducing conditions was a portion of SA-5K released after reduction of a disulphide bridge. The presence of the gene for SA-5K in BCG and its identity were confirmed by PCR (polymerase chain reaction) with specific primers and restriction analysis: the PCR product was slightly shorter in BCG than in *M. tuberculosis*. The gene coding for SA-5K was cloned by PCR from BCG and *M. tuberculosis* DNA and was expressed in *Escherichia coli*.

L16 ANSWER 18 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 15

AN 1998:180827 BIOSIS  
DN PREV199800180827

TI Characterization of antigens recognized by new monoclonal antibodies raised against culture filtrate proteins of *Mycobacterium bovis* bacillus Calmette-Guerin.

AU Freer, G. [Reprint author]; Florio, W.; Dalla Casa, B.; Castagna, B.; Maisetta, G.; Batoni, G.; Corsini, V.; Senesi, S.; Campa, M.

CS Dipartimento di Biomedicina Sperimentale, Infettiva e Pubblica, Universita degli Studi di Pisa, Via S. Zeno 35-39, 56127 Pisa, Italy

SO FEMS Immunology and Medical Microbiology, (Feb., 1998) Vol. 20, No. 2, pp. 129-138. print.  
ISSN: 0928-8244.

DT Article  
LA English  
ED Entered STN: 20 Apr 1998  
Last Updated on STN: 20 Apr 1998

AB Effective protection against *Mycobacteria* tuberculosis may be achieved in experimental animals by immunization with proteins secreted by tuberculous bacilli in the extracellular milieu during growth. In this study, monoclonal antibodies were raised against *Mycobacterium bovis* bacillus Calmette-Guerin (BCG) culture filtrate proteins or live BCG, in an attempt to identify novel mycobacterial secretion antigens: the localization of the antigens recognized by the monoclonal antibodies within the mycobacterial cell was studied and interspecies reactivity was also investigated. The monoclonal antibodies obtained recognized proteins of molecular mass ranging from 5 to 82 kDa, with a prevailing frequency in the 30 kDa region. Three of the monoclonal antibodies recognized proteins present only in culture filtrates. one reacted with a cytoplasmic antigen, while the remaining antibodies recognized components which were mainly associated with the cell wall and the cytoplasmic membrane. The chemical nature and possible identity of the antigens was checked. Three monoclonal antibodies are likely to react with novel mycobacterial antigens of 5, 42 and 82 kDa, respectively.

L16 ANSWER 19 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 16

AN 1999:8557 BIOSIS  
DN PREV199900008557

TI Analysis of the *Mycobacterium bovis* hsp60 promoter activity in recombinant *Mycobacterium avium*.

AU Batoni, Giovanna [Reprint author]; Maisetta, Giuseppantonio; Florio,

CS Walter; Freer, Giulia; Campa, Mario; Senesi, Sonia  
Dip. Patol. Sperimentale Biotechnol. Med. Infettivol. Epidemiol., Univ.  
Pisa, Via S. Zeno 35/39, 56127 Pisa, Italy

SO FEMS Microbiology Letters, (Dec. 1, 1998) Vol. 169, No. 1, pp. 117-124.  
print.

CODEN: FMLED7. ISSN: 0378-1097.

DT Article  
LA English  
ED Entered STN: 11 Jan 1999  
Last Updated on STN: 11 Jan 1999

AB A clinical isolate of *Mycobacterium avium* was transformed with a new shuttle plasmid containing the *Escherichia coli* betagalactosidase reporter gene under the control of the *Mycobacterium bovis* bacillus Calmette-Guerin (BCG) hsp60 promoter. betaGalactosidase activity was assayed spectrophotometrically in bacterial homogenates of the recombinant strain (*M. avium*::lacZ) and used for quantification of the hsp60 promoter strength in different conditions of extra- and intracellular growth. Very low levels of beta-galactosidase were recorded during the exponential phase of in vitro growth, while they increased progressively during the late exponential and stationary phases. A significant increase in enzyme activity was also induced in exponentially growing cells by shifting the incubation temperature from 37 to 45degree C, but not from 37 to 42degree C nor from 30 to 42degree C. No induction of the promoter was observed by adding hydrogen peroxide to the cultures. Finally, beta-galactosidase levels were quantified during growth of *M. avium*::lacZ in murine macrophages. Soon after phagocytosis and, to a lesser extent at 1, 5 and 7 days after infection, increased levels of bacterial beta-galactosidase were observed indicating an increment in transcriptional activity of hsp60 promoter both at early phases of infection and during the course of intracellular growth.

L16 ANSWER 20 OF 20 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN DUPLICATE 17

AN 1997:448540 BIOSIS

DN PREV199799747743

TI Comparative analysis of subcellular distribution of protein antigens in *Mycobacterium bovis* bacillus Calmette-Guerin.

AU Florio, W. [Reprint author]; Freer, G.; Dalla Casa, B.; Batoni, G.; Maisetta, G.; Senesi, S.; Campa, M.

CS Dipartimento di Biomedicina Sperimentale Infettiva e Pubblica, Universita degli Studi di Pisa, Via S.zeno 35-39, I-56127 Pisa, Italy

SO Canadian Journal of Microbiology, (1997) Vol. 43, No. 8, pp. 744-750.  
CODEN: CJMIAZ. ISSN: 0008-4166.

DT Article

LA English

ED Entered STN: 27 Oct 1997

Last Updated on STN: 27 Oct 1997

AB The distribution of protein antigens in purified subcellular fractions of *Mycobacterium bovis* bacillus Calmette-Guerin (BCG) was comparatively analysed by sodium dodecyl sulfate - polyacrylamide gel electrophoresis and immunoblotting with specific monoclonal antibodies and polyclonal sera. The 19- and 38-kDa lipoproteins were mainly detected in the cell wall and cell membrane enriched fractions, and they were extracted from the former by Triton X-114 and Nonidet P-40. The 65-kDa heat-shock protein (hsp) was present in the cytoplasmic fraction and only trace amounts were found in the crude cell wall preparation. In contrast, the 14-kDa hsp was highly represented in the cell wall fraction, besides being present in cytoplasmic fraction. Both superoxide dismutase (SOD) and antigen 85 complex (Ag 85) were abundantly released in culture medium, and to a lower extent, they were present in the cell wall fraction; SOD was present in comparable amounts also in the cytoplasmic fraction, while Ag 85 was far less represented in the same. Sera from mice immunized with culture filtrate (CF) proteins of BCG recognized several antigens in CFs, which were not detectable in cell wall, cell membrane, and cytoplasmic fractions, indicating that CF proteins include secreted antigens which have not yet been identified.

=> s tuberculosis and (RD1-ORF3)

L17

## 9 TUBERCULOSIS AND (RD1-ORF3)

=&gt; dup rem 117

PROCESSING COMPLETED FOR L17

L18 6 DUP REM L17 (3 DUPLICATES REMOVED)

=&gt; d bib ab 1-

YOU HAVE REQUESTED DATA FROM 6 ANSWERS - CONTINUE? Y/(N):y

L18 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

AN 2004:490265 CAPLUS

DN 141:52841

TI Cloning and characterization of genes encoding culture filtrate antigens involved in protective immunity to *M. tuberculosis*, and use thereof as vaccines and in diagnosis

IN Andersen, Peter; Skjot, Rikke; Oettinger, Thomas; Rasmussen, Peter Birk; Rosenkrands, Ida; Weldingh, Karin; Florio, Walter

PA Den.

SO U.S. Pat. Appl. Publ., 109 pp., Cont.-in-part of U.S. 6,641,814.  
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004115211	A1	20040617	US 2003-620246	20030715
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
PRAI	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		
	US 1998-70488P	P	19980105		
	US 1998-50739	A2	19980330		
	DK 1998-1281	A	19981008		
	EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived antigens, isolated from culture filtrates of T cells from memory immune mice by T cell epitope mapping. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, resp. These antigens are suitable for use in vaccines and in diagnosis of infections.

L18 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

AN 2003:696302 CAPLUS

DN 139:229237

TI Protein and DNA sequences of antigens from *Mycobacterium* and uses in *tuberculosis* diagnosis and treatment

IN Andersen, Peter; Weldingh, Karin; Hansen, Christina Vegerby; Florio, Walter; Okkels, Li Mei Meng; Skjot, Rikke Louise Vinther; Rasmussen, Peter Birk

PA Statens Serum Institut, Den.

SO U.S. Pat. Appl. Publ., 53 pp., Cont.-in-part of U.S. Ser. No. 60,428.  
CODEN: USXXCO

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003165525	A1	20030904	US 2002-138473	20020502
	US 6982085	B2	20060103		
	US 6641814	B1	20031104	US 1998-50739	19980330

EP 1449922	A2	20040825	EP 2004-76605	19980401
EP 1449922	A3	20041117		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
US 2002094336	A1	20020718	US 2001-791171	20010220
PRAI DK 1997-376	A	19970402		
US 1997-44624P	P	19970418		
DK 1997-1277	A	19971110		
US 1998-70488P	P	19980105		
US 1998-50739	A2	19980330		
DK 1998-1281	A	19981008		
US 2001-791171	B2	20010220		
US 2002-60428	A2	20020129		
EP 1998-913536	A3	19980401		

AB The present invention is based on the identification and characterization of 9 antigens, including Rv0652/CFP16, Rv2462c/TB51, Rv1984c/CFP21, Rv2185c/TB16, Rv1636/TB15A, Rv3451/CFP23, Rv3872/RD1-ORF3, Rv3354/CFP8A and Rv2623/TB32, from *Mycobacterium tuberculosis*. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as diagnostic reagents containing the polypeptides. The invention related to diagnosing *tuberculosis* caused by virulent mycobacteria, e.g. by *Mycobacterium tuberculosis*, *Mycobacterium africanum* or *Mycobacterium bovis*, in an animal, including a human being. The invention related to treating *tuberculosis* using antigens isolated from *Mycobacterium tuberculosis*.

L18 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3  
AN 2003:609858 CAPLUS  
DN 139:163576  
TI *Mycobacterium tuberculosis* antigens for diagnosis, prevention and treatment of infections caused by species of the *tuberculosis* complex  
IN Andersen, Peter; Skjot, Rikke Louise Vinther  
PA Den.  
SO U.S. Pat. Appl. Publ., 135 pp., Cont.-in-part of U.S. Ser. No. 289,388, abandoned.

CODEN: USXXCO

DT Patent  
LA English  
FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003147897	A1	20030807	US 2001-804980	20010313
	US 6991797	B2	20060131		
	WO 9501441	A1	19950112	WO 1994-DK273	19940701
				W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA	
				RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG	
	EP 1508339	A1	20050223	EP 2004-77505	19940701
				R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI	
	US 5955077	A	19990921	US 1995-465640	19950605
	US 6641814	B1	20031104	US 1998-50739	19980330
	EP 1449922	A2	20040825	EP 2004-76605	19980401
	EP 1449922	A3	20041117		
				R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY	
	US 2002094336	A1	20020718	US 2001-791171	20010220
	US 2004013685	A1	20040122	US 2001-872505	20010601
PRAI	DK 1993-798	A	19930702		
	US 1993-123182	B2	19930920		
	WO 1994-DK273	A2	19940701		
	US 1995-465640	A1	19950605		
	DK 1997-376	A	19970402		
	US 1997-44624P	P	19970418		
	DK 1997-1277	A	19971110		

US 1998-70488P	P	19980105
US 1998-50739	A3	19980330
US 1998-246191	A2	19981230
US 1999-289388	B2	19990412
US 2001-791171	A2	20010220
EP 1994-919574	A3	19940701
EP 1998-913536	A3	19980401
DK 1999-1020	A	19990713
US 1999-144011P	P	19990715
US 2000-615947	A2	20000713
WO 2000-DK398	A2	20000713
US 2001-804980	A2	20010313

AB The present invention is based on the identification and characterization of a number of novel *M. tuberculosis* derived proteins and protein fragments, e.g. TB10.3 (ORF7-1 or Rv3019c), TB10.4 (CFP7 or Rv0288) and TB12.9 (ORF7-2 or Rv3017c), ESAT-6, MPT64, CFP10, RD1-ORF5, RD1-ORF2, Rv1036, Ag85A, Ag85B, Ag85C, 19 kDa lipoprotein, MPT32, MPB59 and  $\alpha$ -crystallin. The invention is directed to the polypeptides and immunol. active fragments thereof, the genes encoding them, immunol. compns. such as vaccines and skin test reagents containing the polypeptides.

L18 ANSWER 4 OF 6 USPATFULL on STN

AN 2003:291011 USPATFULL

TI Nucleic acids fragments and polypeptide fragments derived from *M. tuberculosis*

IN Andersen, Peter, Br.o slashed.nsh.o slashed.j, DENMARK  
Nielsen, Rikke, Frederiksberg, DENMARK  
Oettinger, Thomas, Hellerup, DENMARK  
Rasmussen, Peter Birk, K.o slashed.benhaven, DENMARK  
Rosenkrands, Ida, K.o slashed.benhaven, DENMARK  
Weldingh, Karin, K.o slashed.benhaven, DENMARK  
Florio, Walter, Frederiksberg, DENMARK

PA Statens Serum Institut, Copenhagen, DENMARK (non-U.S. corporation)

PI US 6641814 B1 20031104

AI US 1998-50739 19980330 (9)

PRAI DK 1997-376 19970402

US 1997-44624P 19970418 (60)

DT Utility

FS GRANTED

EXNAM Primary Examiner: Swartz, Rodney P

LREP Frommer Lawrence & Haug, Kowalski, Thomas J.

CLMN Number of Claims: 43

ECL Exemplary Claim: 1

DRWN 6 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 5870

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOS: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L18 ANSWER 5 OF 6 USPATFULL on STN

AN 2002:178550 USPATFULL

TI Nucleic acid fragments and polypeptide fragments derived from *M. tuberculosis*

IN Andersen, Peter, Bronshoj, DENMARK  
Nielsen, Rikke, Frederiksberg C, DENMARK  
Oettinger, Thomas, Hellerup, DENMARK  
Rasmussen, Peter Birk, Kobenhaven O, DENMARK  
Rosenkrands, Ida, Kobenhaven O, DENMARK  
Weldingh, Karin, Kobenhaven N, DENMARK  
Florio, Walter, Frederiksberg C, DENMARK

PA STATENS SERUM INSTITUT (non-U.S. corporation)  
 PI US 2002094336 A1 20020718  
 AI US 2001-791171 A1 20010220 (9)  
 RLI Division of Ser. No. US 1998-50739, filed on 30 Mar 1998, PENDING  
 PRAI DK 1997-376 19970402  
 DK 1997-1277 19971110  
 US 1997-44624P 19970418 (60)  
 US 1998-70488P 19980105 (60)  
 DT Utility  
 FS APPLICATION  
 LREP FROMMER LAWRENCE & HAUG LLP, 745 FIFTH AVENUE, NEW YORK, NY, 10151  
 CLMN Number of Claims: 53  
 ECL Exemplary Claim: 1  
 DRWN 6 Drawing Page(s)  
 LN.CNT 6134  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.  
 AB The present invention is based on the identification and characterization of a number of *M. tuberculosis* derived novel proteins and protein fragments (SEQ ID NOs: 2, 4, 6, 8, 10, 12, 14, 16, 17-23, 42, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72-86, 88, 90, 92, 94, 141, 143, 145, 147, 149, 151, 153, and 168-171). The invention is directed to the polypeptides and immunologically active fragments thereof, the genes encoding them, immunological compositions such as vaccines and skin test reagents containing the polypeptides. Another part of the invention is based on the surprising discovery that fusions between ESAT-6 and MPT59 are superior immunogens compared to each of the unfused proteins, respectively.

L18 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1998:684968 CAPLUS

DN 129:300060

TI Novel antigens of *Mycobacterium tuberculosis* culture filtrates and the genes encoding and their diagnostic and prophylactic use  
 IN Andersen, Peter; Nielsen, Rikke; Rosenkrands, Ida; Weldingh, Karin; Rasmussen, Peter Birk; Oettinger, Thomas; Florio, Walter  
 PA Statens Serum Institut, Den.

SO PCT Int. Appl., 264 pp.  
 CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 10

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9844119	A1	19981008	WO 1998-DK132	19980401
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2285625	AA	19981008	CA 1998-2285625	19980401
	AU 9868204	A1	19981022	AU 1998-68204	19980401
	AU 740545	B2	20011108		
	EP 972045	A1	20000119	EP 1998-913536	19980401
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TT, UA, UG, US, UZ, VN, YU, ZW  
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AB Culture filtrate antigens of *Mycobacterium tuberculosis* are characterized and cDNAs encoding them are cloned. Some of the proteins are antigenic and suitable for use in vaccines and in diagnosis of infections, e.g. skin tests. A fusion protein of two of these antigens is a superior immunogen compared to the unfused proteins. Individual antigens from culture filtrates were identified by T cell mapping using T cells from memory immune mice. Genes for individual antigens were then cloned by screening a λgt11 expression vector with monoclonal antibodies. Manufacture of individual antigens with hexahistidine affinity labels is described.

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